

# EXHIBIT B

UNITED STATES DISTRICT COURT  
FOR THE WESTERN DISTRICT OF TEXAS  
AUSTIN DIVISION

In re CASSAVA SCIENCES, INC.  
SECURITIES LITIGATION

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Master File No. 1:21-cv-00751-DAE

CLASS ACTION

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This Document Relates To:

ALL ACTIONS

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**CONSOLIDATED COMPLAINT FOR VIOLATIONS  
OF THE FEDERAL SECURITIES LAWS**

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Lead Plaintiff Mohammad Bozorgi and additional plaintiffs Ken Calderone and Manohar Rao (together, “Plaintiffs”), individually and on behalf of all others similarly situated, by Plaintiffs’ undersigned attorneys, allege the following based upon personal knowledge as to Plaintiffs and Plaintiffs’ own acts and upon information and belief as to all other matters based on the investigation conducted by Plaintiffs’ attorneys, which included, among other things, a review of the United States Securities and Exchange Commission (“SEC”) filings by Cassava Sciences, Inc. (“Cassava” or the “Company”), conference call transcripts, Company press releases and media reports about the Company, consultation with experts in image analysis and documents obtained through Freedom of Information Act (“FOIA”) or Freedom of Information Law (“FOIL”) requests. Plaintiffs believe that substantial additional evidentiary support will exist for the allegations set forth herein after a reasonable opportunity for discovery.

## **I. INTRODUCTION**

1. This is a securities fraud class action concerning an attempt by corporate executives at Cassava to line their pockets with millions of dollars in compensation and public funding by repeatedly touting an unproven and unlikely potential treatment for Alzheimer’s disease, simufilam (sometimes referred to as PTI-125). But in trumpeting the purported “strong scientific rationale” for their drug, Cassava and its executives concealed that the underlying pre-clinical and clinical studies purportedly justifying the continued commercial development of simufilam contained rampant data manipulation and significant anomalies undermining the validity of the research conducted by two financially conflicted scientists with a previously undisclosed history of scientific misconduct – Dr. Hoau-Yan Wang, Cassava’s primary scientific consultant, and Dr. Lindsay Burns, Cassava’s Senior Vice President of Neuroscience and the wife of Cassava’s founder and CEO, Remi Barbier (“Barbier”).

2. Instead of telling the truth regarding the problematic research supporting the very scientific basis for their drug, Defendants assured investors “[y]ou don’t have to take our word for it. The underlying science is published in a number of peer reviewed journals and benefits from multiple recent clinical and



non-clinical research grants from the [National Institutes of Health (‘NIH’)],” as the Company reported suspect, and certain instances, false and misleading, results. Unsurprisingly, in response to this misinformation, Cassava’s stock price skyrocketed, qualifying Defendants for hundreds of millions of dollars’ worth of cash bonuses tied not to meaningful product development milestones, but short-term increases in Cassava’s stock price under a suspiciously timed executive compensation plan.

3. Yet even after this scheme was brought to light by a pair of intrepid doctors-turned-investors in a “citizen petition” to the United States Food and Drug Administration (“FDA”), rather than properly investigate the facts, Cassava’s leadership recklessly denied the claims out of hand – despite also conceding that their data contained errors – and then attempted to cover up the fraud by submitting doctored data to scientific journals questioning the Company’s research. As the full truth slowly became known, Cassava’s stock price collapsed, damaging investors that had purchased the Company’s securities at artificially inflated levels.

4. Worse, this was not the first time Company executives misrepresented and misstated the prospects of a longshot wonder drug at investor expense. A federal judge previously found that there was evidence that CEO Barbier and other Company executives had lied to investors in a securities fraud class action concerning Cassava’s predecessor entity, Pain Therapeutics, Inc. (“Pain Therapeutics”), and the prospects for the Company’s then-lead product candidate Remoxy. The FDA also reprimanded Pain Therapeutics for misleading marketing practices concerning Remoxy.

5. Today, prominent members of the scientific community have independently validated the citizen petition’s new concerns regarding Cassava and numerous papers authored by Drs. Burns and Wang have been retracted or publicly questioned by scientific journals. As a direct result of the citizen petition, Cassava is currently under criminal and civil investigation by the SEC, United States Justice Department (“DOJ”), and NIH.

6. Starting in 2021, Cassava leapt from relative obscurity to become a favored stock among individual investors, drawn by the prospects for its lead product candidate, simufilam, as a treatment for Alzheimer's disease. During the summer of 2021, the Company's stock price surged to as high as \$146 per share, and eclipsed \$5 billion in market value, despite Cassava having no approved commercial drugs or product revenue. Nevertheless, its stock price increased 911% for the year as of June 2021, and Cassava was the top biotech performer for the year.

7. But the Company didn't have much of a record in Alzheimer's research or developing notoriously difficult to achieve Alzheimer's treatments. In fact, until 2019, just two years prior, Cassava had been named Pain Therapeutics, Inc. and was known primarily for attempting (and repeatedly failing) to develop an opioid painkiller, Remoxy. When the Company failed to gain FDA approval for Remoxy in 2018, the Company lost 98% of its value. It was at that point that Pain Therapeutics undertook a "strategic reorganization" to remake itself as Cassava, a company focused on the treatment of neurodegenerative diseases, such as Alzheimer's.

8. After the rebranding, word began to spread about Cassava on online forums, such as Reddit, and the Company gained popularity among individual retail investors amidst a steady stream of pronouncements from Cassava's management hyping their supposedly groundbreaking new potential Alzheimer's treatment. But in May 2020, the Company acknowledged that the results of an important placebo-controlled Phase 2 clinical trial of simufilam had been unsuccessful – the drug failed to demonstrate efficacy in lowering certain biomarkers of Alzheimer's.

9. Barbier, however, was undeterred. He said that there must have been some mistake, and subsequently announced that the Company had commissioned a reanalysis by a second so-called "outside lab." This time, the data from the do-over showed the exact opposite of the first results – a significant *improvement* in Alzheimer's biomarkers compared to placebo. Following the announcement of these new results from the reanalysis in September 2020, the Company's stock again began to climb, and Barbier and

his fellow Cassava executives qualified for millions of dollars in cash bonuses pegged to short term increases in the Company's stock price – pursuant to an all too conveniently timed executive bonus plan put into place just *weeks* before the Company announced the positive results of the Phase 2 trial reanalysis.

10. Then, in February 2021, Cassava reported purportedly promising results from another trial – this one conducted without any placebo – and claimed that, in an unprecedented breakthrough, simufilam may actually renew cognitive function in Alzheimer's patients. Such studies, however, are prone to the “placebo effect,” which can be particularly strong in Alzheimer's trials, where reported improvements could have been due to positive expectations, as all participants are aware they are receiving the drug. Nevertheless, the stock price reached new heights, and Barbier and his fellow Cassava executives continued to qualify for millions more in cash bonuses as Cassava's stock price climbed.

11. Cassava took advantage of its now skyrocketing stock price to raise \$200 million in gross proceeds in a registered direct stock offering, selling more than four million shares of its common stock at \$49 per share on February 10, 2021, for funding needed to continue simufilam's commercial development and fill the Company's bonus pool.

12. After the close of trading on August 24, 2021, however, reports emerged that the FDA had received a Citizen Petition requesting the FDA halt any future Phase 3 trials of simufilam, pending an audit by the agency (the “Citizen Petition”). As detailed in the Citizen Petition: “[i]nformation available to the petitioner . . . raises *grave concerns* about the quality and integrity of the laboratory-based studies surrounding this drug candidate and supporting the claims for its efficacy.” Of particular concern, the Citizen Petition claimed that the foundational pre-clinical and clinical evidence supporting the continued development of simufilam as a treatment for Alzheimer's had been manipulated, undercutting the prospects that the drug would be an efficacious treatment for the disease.

13. According to the Citizen Petition, Cassava and its principal scientific advisor, Dr. Wang, a professor at the City University of New York (“CUNY”) Medical School, had manipulated and falsified

data in a string of academic journals and presentations providing the basis for the underlying science supporting the continued commercial development of simufilam, including in multiple pieces of self-proclaimed “key” research by Cassava, and concealed that the purported “outside” lab that conducted the Phase 2b reanalysis was none other than Dr. Wang.

14. The next morning, on August 25, 2021, before the market opened, Cassava issued a press release in response to the Citizen Petition, stating, without authenticating the data, that the allegations made in the petition were false and misleading. The Company further claimed that the Phase 2b clinical data the Company had recently presented at a July 26, 2021 Alzheimer’s Association International Conference (“AAIC”) had been generated by Quanterix Corp. (“Quanterix”), an independent company, to suggest that the data presented was correct and valid.

15. Cassava’s attempt to fend off the “grave concerns” raised by the Citizen Petition were unavailing. On August 25, 2021, the Company’s share price plummeted \$36.97 per share, or 31.38%, to close at \$80.86 per share, on unusually heavy trading volume of approximately 29 million shares. The Company’s stock price continued to trade down the next day, August 26, falling \$10.01 per share to \$70.85 per share, on sustained heavy trading volume of 25 million shares.

16. The following day, on August 27, 2021, before the market opened, Quanterix issued its own statement denying the Company’s claims, stating that it “did not interpret the test results or prepare the data” Cassava presented. That same day, Cassava confirmed Quanterix’s statement, stating that “Quanterix[s] sole responsibility with regard to this clinical study was to perform sample testing, specifically, to measure levels of p-tau in plasma samples collected from study subjects.”

17. On this news, the Company’s share price fell \$12.51, or 17.66%, to close at \$58.34 per share on August 27, 2021, again on unusually heavy trading volume of approximately 44 million shares.

18. The negative news regarding the Company, however, continued unabated. A supplement to the Citizen Petition, dated August 30, 2021, identified new instances of scientific misconduct by Cassava

and Dr. Wang, and world renown image analyst Dr. Elisabeth Bik, having picked up on the news of the Citizen Petition, found additional inconsistencies in Cassava’s clinical data.

19. On this news, the Company’s share price fell \$5.08, or 8.7%, to close at \$53.26 per share on August 30, 2021, with over 15.5 million shares of Cassava stock trading.

20. On September 3, 2021, Cassava issued a press release “Cassava Sciences Releases a Public Statement Regarding Recent Allegations” with a transcript of remarks made by Barbier. In the press release, Barbier again denied the accusations in the Citizen Petition, stating, without evidence: “Let me be very clear: I think these allegations are false.” But in his remarks, Barbier admitted that there were “visual errors” in “one publication and one poster presentation” that had been called into question by the Citizen Petition.

21. On this news, Cassava’s stock price fell 7.6%, or \$4.15 per share, to \$50.20 per share, on September 3, 2021, on unusually heavy trading volume of over 27 million shares.

22. With Cassava’s stock in free fall, the Company issued another press release on November 4, 2021, stating that Cassava had “been informed by the *Journal of Neuroscience* that there is no evidence of data manipulation in an article it published in July 2012 describing a new approach to treating Alzheimer’s disease.” According to the release, the *Journal of Neuroscience* requested “raw data for the article, including images of original, uncropped Western blots. Having received that data and completed its review, the *Journal of Neuroscience* stated: “No evidence of data manipulation was found for Western blot data.” With the journal’s apparent exoneration in hand, Barbier stated in the release: “I’ve never doubted the integrity of our people or science.”

23. The November 4, 2021 press release had its intended effect, causing Cassava’s stock price to jump 49%, to \$84.40 per share, that day.

24. Just days later, however, on November 10, 2021, hours after the purported “original” data was made publicly available by the *Journal of Neuroscience*, Dr. Bik reviewed the materials and raised

numerous concerns on Twitter and PubPeer (a website where scientists comment on one another's work). Dr. Bik indicated that the "original" images supplied to the journal were in fact composites of cropped images, and thus, *not the originals at all*.

25. On this news, Cassava's stock price fell 11.5%, or \$9.01 per share, to \$69.40 per share on November 10, 2021.

26. Yet, as Cassava continued to deny all wrongdoing, the negative news continued to trickle out. A little less than one week later, Cassava disclosed in its Form 10-Q for Q3 2021, filed with the SEC on November 15, 2021, that "[c]ertain government agencies have asked us to provide them with corporate information and documents."

27. On this news, Cassava's stock fell another 12%, or \$8.29 per share, to close at \$60.51 per share, on November 15, 2021.

28. Days later, on November 17, 2021, the *Wall Street Journal* published an article which revealed that "[t]he [SEC] is investigating claims that [Cassava], SAVA . . . the sixth-best performing U.S. stock this year, manipulated research results of its experimental Alzheimer's drug, according to people familiar with the matter." The investigation followed an August 2021 meeting between the SEC and the authors of the Citizen Petition. The article also revealed that, according to Barbier, the NIH, which had awarded \$20 million in grants to Cassava, was also examining the claims, and Barbier further confirmed that CUNY had begun a research misconduct inquiry into Dr. Wang.

29. That same day, another supplement to the Citizen Petition, dated November 17, 2021, further revealed that biomarker discrepancies in Cassava's clinical data "are so extreme they suggest lab errors or manipulation," and described findings made by Dr. Adrian Helibut, an investor that had previously taken short positions on Cassava, that experiments supporting simufilam are "seemingly undoable."

30. As a result, Cassava's stock price declined 23.7%, or \$14.62 per share, to \$47.07 per share, on November 17, 2021.

31. On December 9, 2021, a fourth supplement to the Citizen Petition was publicly filed by the FDA. In their supplement, the petition's authors revealed "irrefutable evidence of data manipulation/fabrication" in a fundamental experiment found in Cassava's 2017 *Neurobiology of Aging* paper demonstrating simufilam's purported method of action for treating Alzheimer's disease.

32. On this news, Cassava's stock price closed at \$45.86 per share on December 9, 2021, an 8.2% decline of \$4.12 per share from the prior day's closing price.

33. On December 17, 2021, the *Journal of Neuroscience* changed its "Editorial Note," which had been the subject of the Company's November 4, 2021 press release suggesting that the journal had cleared Cassava scientists of wrongdoing, into an Expression of Concern. The change came after Dr. Bik raised the aforementioned concerns regarding the authenticity of the purported "original data" submitted by the paper's authors. The Expression of Concern stated:

The editors have been made aware of concerns about Western blots in this study, including those published with the article's erratum (Wang et al., 2021). These and other concerns are currently under investigation by the academic authorities at the [CUNY]. *JNeurosci* will await the outcome of that investigation before taking further action.

34. On this news, Cassava's stock price fell 15.6%, or \$6.82 per share, between Friday, December 17 and Monday, December 20, 2021, to close at \$36.77 per share.

35. The December 17, 2021 Expression of Concern, however, would only be the first of many issued by scientific journals in the coming months regarding Drs. Burns's and Wang's research following the Citizen Petition's release. And the scientific community would also go on to find multiple additional instances where Drs. Burns and Wang supplied apparently doctored images to journals attempting to investigate the misconduct in attempts by Cassava and Dr. Wang to cover-up their misdeeds.

36. On December 20, 2021, the journal *Neuroscience* said it found "no evidence" of manipulation in a 2005 paper by Drs. Burns and Wang, after the journal had "asked the authors for images

of the original, uncropped Western blots from this study.” But, as with the *Journal of Neuroscience* paper, when *Neuroscience* publicly released the purported “original” data supplied by the authors, image analysis experts, including Dr. Bik, found extensive evidence of manipulations in the so-called original data, as well.

37. On January 3, 2022, the journal *Molecular Neurodegeneration* retracted a 2021 paper by agreement of its authors due to irregularities found in published data originating from Dr. Wang’s lab. Following the identification of the irregularities, the paper’s corresponding author requested the original blot images from Dr. Wang, but the “original” blot images Dr. Wang supplied *also* had signs of image manipulation. The authors, accordingly, agreed to retract the paper.

38. On March 22, 2022, the journal *Neurobiology of Aging* issued an Expression of Concern regarding a 2017 paper by Drs. Burns and Wang. The journal had found an extensive list of errors in the paper, many of which had been identified by the Citizen Petition. The journal concluded that it would make a final decision regarding corrective action following the conclusion of the ongoing CUNY inquiry into the misconduct.

39. On March 30, 2022, the journal *PLOS One* **retracted five papers** authored by Drs. Wang and Burns. For each of the five papers, two of which Drs. Wang and Burns authored together and the remaining three Dr. Wang authored with others, the journal stated: “The data and comments provided to PLOS ***did not resolve the concerns about the integrity and reliability of the reported data.***” In light of these issues, PLOS ONE retracted each article.

40. On April 18, 2022, *The New York Times* published a wide-ranging exposé on Cassava, in which reporters interviewed nine “prominent experts for comment about the scientific underpinnings of Cassava’s trials.” According to the newspaper, “[a]ll said they did not trust the company’s methods, results or even the premise underlying the drug’s supposed effectiveness.”



41. On this news, Cassava's stock price fell 11.3%, or \$4.92 per share, on April 19, 2022, to \$22.46 per share, and continued falling the following day, another 9.2%, to \$20.39 per share, on April 20, 2022.

42. On June 1, 2022, the journal *Alzheimer's Research & Therapy* retracted a 2017 paper published by Dr. Wang and others. The retraction noted that "[f]ollowing publication, concerns have been raised regarding the western blot images presented in Figs. 1, 5 and 6." Once again, though the authors supposedly provided the raw data to addresses the concerns, independent experts deemed that data "insufficient to address" the issue. As a result, the editors-in-chief of the journal no longer had "confidence in the integrity of the data" and retracted the article.

43. On this news, Cassava's stock price fell 12.4%, or \$3.78 per share, on June 1, 2022, to \$26.82 per share.

44. Finally, on July 27, 2022, prior to market open, *Reuters* published a story disclosing that the DOJ "opened a criminal investigation into Cassava . . . involving whether the biotech company manipulated research results for its experimental Alzheimer's drug." According to the news outlet:

The [DOJ] personnel conducting the investigation into Austin, Texas-based Cassava specialize in examining whether companies or individuals have misled or defrauded investors, government agencies or consumers.

45. On this news, Cassava's stock price fell 14%, or \$3.03 per share, on July 27, 2022, to \$18.69 per share.

## **II. NATURE OF THE ACTION**

46. This is a securities fraud class action on behalf of all purchasers or acquirers of Cassava securities between September 14, 2020 and July 26, 2022, inclusive (the "Class Period"), seeking to pursue remedies under §§10(b) and 20(a) of the Securities Exchange Act of 1934 (the "Exchange Act"), as amended by the Private Securities Litigation Reform Act of 1995 ("PSLRA") and Rule 10b-5 promulgated thereunder (17 C.F.R. §240.10b-5).

47. As a result of Defendants' wrongful acts and omissions as alleged herein, Plaintiffs and the Class (as defined below) purchased or acquired Cassava securities at artificially inflated prices, suffered significant losses, and were damaged thereby.

### III. JURISDICTION AND VENUE

48. The claims asserted herein arise under and pursuant to §§10(b) and 20(a) of the Exchange Act, 15 U.S.C. §§78j(b) and 78t(a), and Rule 10b-5, 17 C.F.R. §240.10b-5, promulgated thereunder by the SEC.

49. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §1331 and §27 of the Exchange Act.

50. Venue is proper in this District pursuant to §27 of the Exchange Act and 28 U.S.C. §1391(b). Many of the acts charged herein, including the preparation and dissemination of materially false and misleading information, occurred in substantial part in this District where Cassava is headquartered.

51. In connection with the acts alleged in this complaint, Defendants, directly or indirectly, used the means and instrumentalities of interstate commerce, including, but not limited to, the mails, interstate telephone communications, and the facilities of the NASDAQ.

### IV. THE PARTIES

52. **Lead Plaintiff Mohammad Bozorgi:** As set forth in the amended certification attached hereto as Exhibit A, Bozorgi purchased Cassava common stock during the Class Period and suffered damages as a result of the federal securities law violations, false and/or misleading statements, and/or material omissions alleged herein. Bozorgi's losses from Class Period transactions in Cassava stock total over \$1.7 million, as of August 16, 2022.

53. **Additional Plaintiff Ken Calderone:** As set forth in the certification attached hereto as Exhibit B, Calderone purchased Cassava securities during the Class Period, and suffered damages as a

result of the federal securities law violations, false and/or misleading statements, and/or material omissions alleged herein. Calderone's losses from Class Period transactions in Cassava securities total over \$100,000, as of August 5, 2022.

54. **Additional Plaintiff Manohar K. Rao:** As set forth in the amended certification attached hereto as Exhibit C, Rao purchased Cassava securities during the Class Period, and suffered damages as a result of the federal securities law violations, false and/or misleading statements, and/or material omissions alleged herein. Additionally, Rao has been assigned the rights and interests of his wife and his sister-in-law who also purchased Cassava securities during the Class Period. ECF 17-5 at ¶3. Rao's losses from Class Period transactions in Cassava securities total over \$597,000.

55. **Defendant Cassava:** Cassava was incorporated in 1998 as Pain Therapeutics, Inc. and changed its name to Cassava Sciences, Inc. in March 2019. The Company is headquartered in Austin, Texas. During the Class Period, Cassava common stock traded in an efficient market on the NASDAQ under the ticker symbol "SAVA." As of August 2, 2021, there were more than 40 million shares of Cassava common stock issued and outstanding.

56. Cassava is a small company. Between 2012 and 2019 Cassava had eight to nine employees. By year-end 2020, Cassava had just 11 full-time employees. During the Class Period, the Company was focused on the development of Cassava's primary product candidate, simufilam, as a treatment for Alzheimer's disease.

57. At all relevant times, Cassava retained **Hoau-Yan Wang**, Ph.D., an Associate Medical Professor at CUNY Medical School, as a Company consultant and member of its scientific advisory board. In Company presentations, Dr. Wang is described as the "*co-lead scientist* on discovery & development of PTI-125" and the Company's "*principal scientific collaborator*." Dr. Wang is listed as a co-author on Cassava presentations filed with the SEC alleged to be false and misleading. In SEC filings, Dr. Wang is also listed as part of the Company's product development team as one of Cassava's scientific advisors.

58. In the November 17, 2021 *Wall Street Journal* article, Barbier confirmed that “Cassava pays Dr. Wang as a consultant.” Documents produced by CUNY pursuant to a FOIL request further confirm that Dr. Wang expected to receive at least \$24,000 from Cassava in 2021 and that he held \$125,000 in Cassava stock or stock options. According to news reports, Dr. Wang also participates in an unspecified Cassava bonus plan.

59. **Defendant Remi Barbier:** Since founding the Company in 1998, Barbier has been Chairman, President, and CEO of Cassava, and its predecessor, Pain Therapeutics, where he has “global responsibilities for the scientific direction, management, operations, strategy, and financing of the Company,” as described in documents Cassava submitted to the NIH. Barbier is a member of Cassava’s product development and management teams and, in a June 8, 2021 *Fortune* article “Cassava Sciences – a drugmaker with no products on the market – is currently 2021’s best biotech performer,” Barbier boasted: “*I know* the science, *I know* the data, I know the disease and this stuff looks promising and I’m putting my money where my mouth is.”

60. During the Class Period, Barbier spoke on Cassava’s behalf in press releases, conference calls, and SEC filings and is listed as a co-author on certain Company research related to simufilam that has been both published in scientific journals and in Company presentations filed with the SEC alleged to be false and misleading herein. Barbier also participated in the Company’s cash incentive bonus plan during the Class Period, which qualified him to receive millions of dollars in compensation based on short-term increases in Cassava’s stock price, unrelated to any drug development milestone. Barbier reviewed and approved the Company’s public statements during the Class Period.

61. **Defendant Lindsay Burns:** Since 2002, Dr. Burns has worked at Cassava (formerly Pain Therapeutics). She currently serves as Cassava’s Senior Vice President of Neuroscience and is a member of its product development and management teams. She has been married to Barbier since at least 2006. In documents Cassava submitted to the NIH, she describes herself as the “project leader on [Cassava’s]

Alzheimer’s program” since the time her “academic collaborator, Dr. Hoau-Yan Wang, identified filamin A (FLNA) as a novel therapeutic target.” She “*monitored the proof-of-concept research, lead selection and efficacy experiments for PTI-125 and oversaw IND-enabling studies, chronic toxicity studies, and first-in-human and first-in-patient clinical trials.*”

62. Burns also wrote:

... four papers on PTI-125, the first in the *Journal of Neuroscience* in 2012, the second in *Neurobiology of Aging* in 2017, a review paper in a 2017 special issue on [Alzheimer’s disease] in *Neuroimmunology and Neuroinflammation*, and the biomarker results of the Phase 2a clinical trial in [the *Journal of Prevention of Alzheimer’s Disease*].

She “continue[s] to work closely with Dr. Wang and Dr. [Ben] Thornton [a Cassava employee] in the development of SavaDX” and has published at least nine papers with Dr. Wang between 2005 and 2020.

63. During the Class Period, Dr. Burns spoke on Cassava’s behalf on conference calls. Given that, at all relevant times, Dr. Burns led Cassava’s Alzheimer’s program, was a member of the Company’s management team, spoke on the Company’s behalf during conference calls, and was listed as an author on Company presentations regarding simufilam filed with the SEC, it can be inferred that she reviewed and edited the Company’s public statements concerning simufilam during the Class Period.

64. **Defendant Nadav Friedmann:** Since 2001, Dr. Friedmann has served as the Chief Operating Officer and Chief Medical Officer of Pain Therapeutics and then Cassava. He is described in documents submitted by Cassava to the NIH as “overseeing the clinical development of our very promising compound PTI-125.” Dr. Friedmann also served as a member of Cassava’s Board of Directors at all relevant times. During the Class Period, Dr. Friedmann was a member of Cassava’s product development and management teams, and he spoke on Cassava’s behalf in press releases, conference calls, and SEC filings.

65. Given that, during the Class Period, Dr. Friedmann oversaw the clinical development of simufilam, was a member of the Company’s management team and its Board of Directors, spoke on the Company’s behalf during conference calls and press releases, signed Cassava SEC filings and co-authored

Company research, it can be inferred that he reviewed and edited the Company's public statements during the Class Period.

66. Dr. Friedmann also participated in the Company's cash incentive bonus plan during the Class Period, which qualified him to receive millions of dollars in compensation based on short-term increases in Cassava's stock price, unrelated to any drug development milestone.

67. **Defendant Eric J. Schoen:** Schoen has served as Cassava's Chief Financial Officer ("CFO") since October 31, 2018. During the Class Period, Schoen spoke on Cassava's behalf during conference calls and signed Company press releases and SEC filings. Accordingly, it can be inferred that he reviewed and approved Cassava public statements during the Class Period.

68. Schoen participated in the Company's cash incentive bonus plan during the Class Period, which qualified him to receive millions of dollars in compensation based on short-term increases in Cassava's stock price, unrelated to any drug development milestone.

69. Defendants Barbier, Burns, Friedmann, and Schoen are sometimes collectively referred to herein as the "Individual Defendants." The Individual Defendants made, or caused to be made, false or misleading statements that caused Cassava securities to trade at artificially inflated prices during the Class Period. The Individual Defendants, because of their positions with the Company, possessed the power and authority to control the contents of Cassava's press releases, interim financial reports, and presentations to securities analysts and institutional investors, *i.e.*, the market. They were provided with copies of the Company's reports and press releases alleged herein to be misleading prior to or shortly after their issuance and had the ability and opportunity to prevent their issuance or cause them to be corrected. Because of their positions within the Company and their access to material non-public information available to them but not to the public, the Individual Defendants knew that the adverse facts specified herein had not been disclosed to and were being concealed from the public and that the positive representations being made were

materially false and misleading. The Individual Defendants are liable for the false and misleading statements pleaded herein.

70. Cassava and the Individual Defendants are sometimes collectively referred to herein as the “Defendants.”

71. During the Class Period, Defendants are liable for: (i) making false statements; or (ii) failing to disclose adverse facts known to them about Cassava. Defendants’ fraudulent scheme and course of business that operated as a fraud or deceit on purchasers or acquirers of Cassava securities was a success, as it: (i) deceived the investing public regarding Cassava’s prospects and business; (ii) caused the price of Cassava securities to trade at artificially inflated prices, and qualified Defendants to earn, in total, hundreds of millions of dollars in cash bonuses; (iii) permitted Cassava to sell \$275 million of Cassava common stock at fraud-inflated prices; and (iv) caused Plaintiffs and other members of the Class to purchase or acquire Cassava securities at artificially inflated prices.

72. Each of the Individual Defendants is liable as a participant in a fraudulent scheme and course of business that operated as a fraud or deceit on purchasers or acquirers of Cassava securities by engaging in the violative conduct alleged herein, which caused Cassava securities to trade at artificially inflated prices during the Class Period.

## **V. SUBSTANTIVE ALLEGATIONS**

### **A. Cassava Sciences**

73. Cassava is a small Austin, Texas-based clinical stage biotechnology company currently engaged in the development of drugs for the treatment of neurodegenerative diseases, such as Alzheimer’s. Cassava, however, was not always in the business of developing Alzheimer’s drugs.

74. The Company began operations in 1998 as Pain Therapeutics, Inc. As Pain Therapeutics, the Company spent years attempting to bring its then-primary drug candidate, Remoxy (a form of oxycodone that Remi Barbier named after himself) to market. As early as 2003, however, Sidney Wolfe,

of the watchdog group Public Citizen, warned that Remoxy “‘sounds too good to be true.’” He turned out to be right. After four attempts to earn FDA approval, Pain Therapeutics announced on August 6, 2018, that it had received a Complete Response Letter from the FDA denying its Remoxy New Drug Application (“NDA”). According to the FDA, “[t]he data submitted in [the] NDA do not support the conclusion that the benefits of [Remoxy] Extended-Release Capsules outweigh the risks.”

75. With its primary drug candidate a failure, and its stock price having lost nearly all of its value, Pain Therapeutics underwent a “strategic reorganization,” setting out in an entirely new direction to “align its resources on advancing its drug and diagnostic assets in Alzheimer’s disease.” The re-branding could not have come at a better time; the Company was running out of money. As of December 31, 2018, Cassava had just \$19.8 million of cash and cash equivalents and no product revenue. On March 26, 2019, Pain Therapeutics announced it officially changed its name to Cassava Sciences, Inc. – named after the street in the tony Austin neighborhood where Barbier resides, though the Company reported that the new name “was chosen to better reflect the Company’s strategic focus on drug development for neurodegenerative diseases, such as Alzheimer’s disease.”

76. Cassava, however, had “a limited operating history” in its new business targeting Alzheimer’s disease and “no history of product approvals for commercial sale” in any drug according to Company SEC filings, let alone for notoriously difficult to develop Alzheimer’s treatments. Given the Company’s prior history, certain industry commentators were skeptical of the Company’s pivot. According to reporting by STAT, a health-oriented news outlet, Barbier had “a reputation for profiting personally even while his company suffered multiple setbacks.” The October 2, 2020 article, entitled “Failure has paid handsomely for Cassava Sciences’ CEO. His latest cash grab is a risky Alzheimer’s drug,” described:

In the decade between 2008 and 2018, when Cassava was known as Pain Therapeutics, its lead opioid product was rejected by the [FDA] four times. The painkiller was called Remoxy – Barbier named it after himself.



The company's stock price lost 98% of its value over those 10 years, but Barbier, as CEO, earned nearly \$27 million in salary, bonuses, and stock option grants, according to SEC filings.

Barbier couldn't manage to secure the approval of a painkiller, despite four attempts, but he still got rich off shareholder money.

77. Pain Therapeutics had indeed been an unmitigated disaster for investors. In the decades since Barbier founded the Company, the stock traded as high as \$168 per share in September of 2000 before falling to under a dollar-a-share in August 2018, following the FDA's Complete Response Letter. During that time, Barbier and other Company executives, including Dr. Friedmann, were sued for securities fraud in a case that settled near trial after Senior United States District Judge Sam Sparks for the Western District of Texas denied defendants' motion for summary judgment, finding there was sufficient evidence for a jury to reasonably find that Barbier and Friedmann knowingly misled investors concerning whether problems raised by the FDA regarding Remoxy had been resolved. *See KB Partners I, LP v. Pain Therapeutics, Inc.*, No. A-11-CA-1034-SS (W.D. Tex. 2011).

78. The STAT article further noted: "[A]fter the FDA rejected Remoxy for the fourth time, Barbier took no responsibility, neither personally nor on behalf of the company. Instead, he blamed the FDA, accusing regulators publicly of making mistakes and misrepresenting clinical data. 'We can't work with shambolic regulations,' he said."

79. Barbier, however, insisted that his Alzheimer's drug was a different story. Scientists affiliated with the Company had published papers in peer-reviewed journals. Indeed, the March 27, 2019 press release announcing Pain Therapeutics' rebranding into Cassava touted that "[t]he underlying science for our programs in neurodegeneration is published in several prestigious, peer-reviewed technical journals, including Journal of Neuroscience, Neurobiology of Aging, and Journal of Biological Chemistry." In the months and years the followed, the Company continued to laud its pre-clinical published work as forming the basis of Cassava's science and the justification for its advancement as a potential treatment for Alzheimer's.

**B. Cassava’s Lead Product Candidate Simufilam**

80. Cassava’s lead product candidate, simufilam, is an experimental small molecule drug for the treatment of Alzheimer’s disease. Cassava also has a secondary investigational diagnostic product candidate, SavaDx, a blood-based biomarker/diagnostic to detect Alzheimer’s disease. According to Cassava SEC filings, both simufilam and SavaDx were “discovered and designed in-house” at Cassava during research activities that were conducted from approximately 2008 to 2018.

81. An effective treatment for Alzheimer’s could be a blockbuster drug. The World Health Organization reports that more than 50 million people worldwide suffer from the deterioration of memory, thinking, and behavior that is associated with dementia, and Alzheimer’s is the most common type of dementia, representing 60% to 70% of dementia patients. Analysts at Maxim Group estimated that, if successful, simufilam could generate \$2 billion in annual revenue by 2027 and nearly \$5 billion by 2031. Other analysts at Cantor Fitzgerald estimated that, if successful, simufilam could generate nearly \$10 billion in annual revenue by 2033.

82. Since the Company commenced operations in May 1998, however, neither Cassava, nor its predecessor, Pain Therapeutics, have produced a single drug approved for commercial sale or generated any revenue from product sales. According to Company SEC filings, Cassava has rather incurred “significant net losses in each period since [its] inception.” Cassava is therefore “heavily dependent on the success of simufilam and SavaDx,” and if these “product candidates do not receive regulatory approval, [Cassava] will be unable to generate product revenue.”

83. Simufilam, in particular, aims to restore a protein, filamin A (sometimes referred to as “FLNA”), that Cassava’s scientists say is misshaped in the brains of Alzheimer’s patients. In its contorted state, according to Cassava, the protein triggers a toxic process that leads to the buildup in the brain of another protein called amyloid, which is a hallmark of Alzheimer’s disease said to cause the plaques and

tangles found in the brains of people with Alzheimer's. By binding to filamin A, Cassava claims that simufilam could prevent and reverse amyloid-related Alzheimer's disease-related damage.

84. More specifically, according to Cassava, by binding to filamin A, simufilam supposedly reduces abnormal signaling of the  $\alpha 7$ -nicotinic acetylcholine receptor (" $\alpha 7$ nAChR"), reducing toxic amyloid and neuroinflammation in the brain. The entire basis for these claims are experiments conducted by Cassava and Dr. Wang. No other lab has replicated Cassava's putative findings regarding simufilam or a connection between filamin-A function in Alzheimer's disease.

85. As described in Cassava SEC filings, the "[*key*]" elements of Cassava's business strategy to develop simufilam as a treatment for neurodegeneration included "validating our unique scientific approach with competitive research grants and ***publishing our scientific data in peer-reviewed journals.***"

86. According to Cassava's "drug discovery" timeline, simufilam's development began with foundational "basic research" in 2008. Drs. Burns's and Wang's 2008 paper, published in *PLOS-One* (and later retracted by the journal), entitled "High-Affinity Naloxone Binding to Filamin A Prevents Mu Opioid Receptor-Gs Coupling Underlying Opioid Tolerance and Dependence," presented scientific data that "the opioid receptor antagonists naloxone and naltrexone bind a specific site on FLNA with high affinity," which lead to the later purported discovery that FLNA-binding compounds could disrupt the association between FLNA and  $\alpha 7$ nAChR, culminating in the development of Cassava's lead product candidate, simufilam, in and around 2011, to target FLNA and restore its normal shape and function as a potential treatment for Alzheimer's disease.

87. Drs. Burns and Wang then began testing simufilam in animal models, which supposedly "resulted in dramatic improvements in brain health, such as reduced amyloid and tau deposits, improved receptor signaling and improved learning and memory." Drs. Burns and Wang would go on to publish their scientific data on simufilam in many more peer-reviewed journals, including certain "key" publications validating the Company's so-called "unique scientific approach," such as:

- “Altered filamin A enables amyloid beta-induced tau hyperphosphorylation and neuroinflammation in Alzheimer’s disease,” *Neuroimmunology and Neuroinflammation* 2017;
- “PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer’s disease pathogenesis,” *Neurobiology of Aging* 2017;
- “Reducing amyloid-related Alzheimer’s disease pathogenesis by a small molecule targeting filamin A,” *Journal of Neuroscience* 2012; and
- “PTI-125 reduces amyloid-related Alzheimer’s pathogenesis by targeting filamin A,” *Alzheimer’s & Dementia* 2012.

88. Cassava used certain of these “key” pre-clinical studies to garner NIH grants and to open an Investigational New Drug (“IND”) application in 2017 to study simufilam in Alzheimer’s patients. Indeed, a July 31, 2017 Company press release announcing that the FDA had approved the IND specifically named three of the journals noted above, stating: “The underlying science for PTI-125 has been published in *Journal of Neuroscience*, *Neurobiology of Aging*, *Journal of Biological Chemistry*, *PLOS-One* and other peer-reviewed scientific journals.” Following IND approval, Cassava began initial Phase 1 clinical testing to assess simufilam’s tolerability in humans. Cassava then proceeded to Phase 2 studies, including its first placebo-controlled trial to assess simufilam’s efficacy.

### **C. Cassava’s Phase 2b Trial Reanalysis Following Unsuccessful Results**

89. In September 2019, Cassava undertook its first placebo-controlled, blinded trial – a Phase 2b study – to assess simufilam’s efficacy. In this study, funded by the NIH, 64 patients were randomized to receive one of two doses of simufilam or a placebo for 28 days, with a primary endpoint of improvement in biomarkers of Alzheimer’s disease from baseline to day 28, and an assessment of cognitive faculties by episodic memory and spatial working memory tests versus placebo.

90. But on May 15, 2020, Cassava announced simufilam was unable to lower levels of tau protein and other biomarkers detected in the cerebrospinal fluid of patients with Alzheimer’s in the Phase 2b study. Cassava’s press release stated: “Cassava Sciences, Inc. (Nasdaq: SAVA) today reported top-line

results from a Phase 2b study of PTI-125, its lead investigational drug, in patients with Alzheimer's disease. This study did not meet its primary endpoint."

91. When Cassava announced the failure of the Phase 2b study, its stock price fell sharply, and the Company's future was again uncertain. Analysts at H.C. Wainwright & Co. wrote that "the disappointing tau results in this study create uncertainty about PTI-125's prospects for future clinical advancement." Other analysts at Maxim Group advised "a miss is a miss and the path forward for PTI-125 is unclear." But due to a well-timed change in the Company's executive compensation plan, the Individual Defendants were incentivized to pump up Cassava's stock price following the unsuccessful Phase 2b results.

92. Just as when Remoxy suffered development setbacks, when simufilam showed no effect on biomarkers for Alzheimer's disease in the Phase 2b trial, Barbier refused to accept the negative result. Instead, he accused the laboratory that analyzed the cerebrospinal fluid samples of shoddy work. The failed study was the lab's fault, not the drug, Barbier claimed.

93. Cassava then hired a different unnamed "outside" lab to analyze patient samples a second time, noting in a September 14, 2020 press release announcing the results of the reanalysis that "[a]ll CSF samples were sent to *outside labs* for bioanalysis." This time, remarkably, the results were positive for simufilam, showing significant reductions in tau protein and other biomarkers of Alzheimer's disease compared to placebo.

94. Curiously, however, Cassava offered no evidence that the first lab failed to follow correct procedures or conducted its analyses improperly. Indeed, Cassava accepted the first lab's analysis of CSF samples at baseline, and, furthermore, Cassava was happy to rely on the lab's favorable CSF IL-1beta analysis and report those results in the Company's initial May 15, 2020 press release, noting "PTI-125 significantly reduced a secondary endpoint, CSF levels of IL1-beta ( $p < 0.035$ ), a core biomarker of neuro-inflammation, from baseline to Day 28." Cassava's after-the-fact dissatisfaction with the first lab reflects

that the Company only deemed the lab's analysis to be inadequate after receiving undesired results. Emails produced by the NIH pursuant to a FOIA request later revealed that the original lab work was conducted by a lab at Lund University, a public research university in Sweden consistently ranked as one of the best in the world.

95. In addition to the September 14, 2020 press release, Cassava also held an "update call" with analysts and investors that day, presented by Barbier and Drs. Burns and Friedmann, regarding the results of the Phase 2b reanalysis. During the presentation Barbier represented that the second Phase 2b analysis had been done by an "academic lab" and that Cassava and its "outside advisors" had confirmed the second analysis was the "valid analysis." But when asked by an investor whether the first lab ever admitted any mistakes were made in their analysis, Barbier demurred.

96. When asked if the first lab stood by its results, or whether the lab agreed with the Company that its work was faulty, Barbier replied: "Clearly, mistakes were made on their behalf." "Like a lot of parties these days, it's hard for anyone to fess up exactly what happened and when and who did what." Barbier added: "We did our inquiries, we did our forensic inquiries, we clearly see mistakes, others who've seen the data say it's not possible to generate this data, and so we really rely exclusively on the second bioanalysis from this study." The only evidence, however, offered by Cassava that the reanalysis was accurate was because it was positive for simufilam. Moreover, Cassava did not disclose: (i) that, as Barbier would later confirm, the so-called "outside" lab that conducted the reanalysis was none other than Dr. Wang; or (ii) that the reanalysis results were themselves highly anomalous.

97. Following Cassava's announcement of this "do-over," the Company's stock price more than doubled to over \$7 per share. The stock continued to climb higher thereafter, closing at \$11.51 per share, by September 30, 2020. Analysts reacted favorably as well, but remained puzzled by the reanalysis. According to Cantor Fitzgerald in a October 22, 2020 report entitled "Savvy New Target for Neurodegenerative Diseases with Provocative, Early, Clinical Data: Initiating at OW & \$24 PT," the

“[k]ey” “[r]easons to buy SAVA stock” now included “that the *preclinical, P2a, & P2b studies* with [simufilam] show *consistent & provocative results*, which increases the PoS for a P3 study, soon to be initiated.” Yet, they also noted that the “[r]eanalysis of duplicate samples for the P2b of [simufilam] in AD pts remains a question mark.”

#### **D. Cassava’s Bonus Plan**

98. Barbier and other Cassava executives stood ready to cash in on the Phase 2b study reanalysis. On August 26, 2020 – a little more than two weeks before unveiling the revised Phase 2b data on September 14, 2020 – Cassava’s board approved a “cash incentive bonus plan” for its executives, according to a Form 8-K filed with the SEC on September 1, 2020. According to email obtained pursuant to a FOIL request, Dr. Wang began providing Dr. Burns biomarker data on the reanalysis as early as June 12, 2020.

99. In other words, the Defendants knew the results of the reanalysis and then entered into the bonus plan just before publicly announcing the supposedly positive results of the reanalysis in the September 14, 2020 press release, ensuring they would benefit. Moreover, Defendants were incentivized to announce positive results, as negative Phase 2b results likely would have ended further development of simufilam as a treatment for Alzheimer’s disease.

100. Under the bonus plan, if the Company’s market capitalization exceeded \$200 million for 20 consecutive business days, Barbier along with Dr. Friedmann, Schoen, and the Company’s independent directors would split a cash bonus pool of \$10 million. Barbier would get one-third of the bonus cash, so his take would be \$3.3 million of a \$10 million bonus pool. Dr. Friedmann’s and Schoen’s cash bonus would be determined by the Compensation Committee of the Board as a portion of 33.3% and 23.3%, respectively, of the aggregate bonus payment, after taking into account the recommendations of Barbier. Each independent director’s cash bonus would be equal to 2% of the aggregate bonus payment, subject to a reasonable increase for Board committee members.

101. Following the unveiling of the new Phase 2b results, Cassava’s market capitalization topped \$200 million for 20 consecutive business days on October 13, 2020, and “the Company achieved the first Valuation Milestone.” Subsequently, Cassava’s Compensation Committee “approved a cash bonus award of \$7.3 million in total for all Plan participants,” though the award has yet to be paid out.

102. But that was only the first of multiple cash bonuses the executives could obtain through the plan. The plan also awarded additional cash bonuses, triggered by further increases in Cassava’s market capitalization. Cassava’s August 4, 2021 Form 10-Q for the second quarter 2021 stated: “if the Company exceeds a \$5 billion market capitalization for no less than 20 consecutive trading days, all Valuation Milestones would be deemed achieved, in which case cash bonus awards would range from a minimum of \$134.2 million up to a maximum of \$322.3 million.” Under the bonus plan, Barbier could receive as much as \$108 million if all valuation milestones were met.

103. Since the first \$200 million valuation milestone was triggered, Barbier, Friedmann, and Schoen have since qualified to make millions of dollars more in future bonus payments by pumping Cassava’s market value even higher. During the six months ended June 30, 2021, the Company’s market capitalization increased substantially. These increases triggered the achievement of 10 additional plan milestones. Collectively, the achievement of these milestones qualified the plan participants, including Barbier, Friedmann, and Schoen, for bonuses ranging from a minimum of \$81 million up to a maximum of \$195 million, with exact amounts to be determined by Cassava’s Compensation Committee, provided that the Company has sufficient funds to pay them. The bonuses would also be paid out in the event of a merger or acquisition resulting in a change of control. Subsequent to June 30, 2021, the Company achieved one additional milestone triggering potential Company obligations to all plan participants from a minimum of \$12.7 million up to a hypothetical maximum of \$30.0 million.

104. Dr. Wang – the man running Cassava’s “outside” lab – was also a participant in an unspecified Cassava bonus plan, according to a January 17, 2022 *New Yorker* article. When journalists at



the *New Yorker* asked Barbier whether it was appropriate for Dr. Wang to be included in a bonus plan based on short term fluctuations in Cassava's stock price, Barbier said that this was standard practice. But when the same question was posed to Bob Gussin, a former Johnson & Johnson executive who sits on Cassava's Board, he said "[i]t's not typical, I'll say that. And I'm not thrilled with that aspect of things."

#### **E. A Citizen Petition Filed with the FDA Finds Wide-Ranging Data Manipulation in the Foundational Studies Supporting Simufilam**

105. On or about August 18, 2021, a New York attorney, Jordan A. Thomas, filed the Citizen Petition with the FDA on behalf of then-unnamed individuals, citing "*grave* concerns about the quality and integrity of the laboratory-based studies surrounding this drug candidate." The petition contained a 42-page technical report, later revealed to have been created by two scientists, Drs. David Bredt and Geoffrey Pitt, outlining "a series of anomalies" in Cassava's published research "that *strongly suggests systemic data manipulation.*"

106. As the Citizen Petition explained,

[a]ll of the foundational science supporting Cassava's claims about Simufilam's use for Alzheimer's Disease comes from a series of papers with two common co-authors (Dr. Hoau-Yan Wang at CUNY and Dr. Lindsay Burns of Cassava). The studies of Drs. Wang and Burns were used by Cassava to obtain NIH grants and to open an [IND] application to study Simufilam. They form the foundation for the current clinical trials of Simufilam.

No other lab has confirmed Cassava's research connecting Filamin A to Alzheimer's Disease, nor has any other lab confirmed that Simufilam binds or modifies Filamin A or has effects in Alzheimer's Disease models.

107. After a "close review" of the data and analyses in these foundational research papers and Cassava's recent publications of clinical trial analysis, the Citizen Petition authors presented three primary areas of concern:

- ***First***, the underlying papers of Drs. Wang and Burns involve extensive use of Western blot analysis to support their claims connecting Simufilam to Alzheimer's. Detailed analysis of the western blots in the published journal articles shows a series of anomalies that are *strongly suggestive of systematic data manipulation and misrepresentation.*

- **Second**, Cassava’s presentation of clinical biomarker data from that Phase 2b trial raises questions about the validity of the data. The CSF samples in this study were first analyzed by an outside lab, which found that Simufilam was ineffective in improving the primary biomarkers end point and high variability in other biomarkers. But Cassava had these samples analyzed again and this time reported that Simufilam rapidly and robustly improved a wide array of biomarkers. Cassava has not fully published the data from this reanalysis, but a presentation posted that it published on July 26, 2021, which appears to describe aspects of that work, shows signs of *data anomalies or manipulation*.
- **Third**, some of the foundational studies published by Drs. Wang and Burns make claims about Simufilam’s effects in experiments conducted on postmortem human brain tissue. The methodology allegedly used in these experiments defied logic, and the data presented again have *hallmarks of manipulation*.

108. The petition highlighted that for over 15 years, Cassava (and previously Pain Therapeutics) funded Dr. Wang’s lab at CUNY, and that Drs. Wang and Burns have together published nearly a dozen papers that purported to connect filamin A with pain and Alzheimer’s disease.

109. During that time, the petition detailed “a *long-standing pattern of seemingly intentional data manipulation and misrepresentation in scientific papers and corporate disclosures* authored primarily by Drs. Hoau-Yan Wang, Associate Medical Professor [CUNY], and Lindsay A Burns, Sr. Vice President of Neuroscience at Cassava Sciences.” These “apparent falsifications have helped garner >\$5,000,000 in NIH grants for preclinical/clinical studies, attract >\$250,000,000 in public fundraising by Cassava Sciences and misdirect therapeutic studies for patients suffering from Alzheimer’s Disease (AD).”

110. Shortly after the Citizen Petition was publicized, members of the scientific community began reviewing the petition’s findings and validating the concerns it raised, as well as identifying “new errors and anomalies that strongly suggest scientific misconduct in their reports about both preclinical and clinical data,” as the petition’s authors wrote in a supplement filed with the FDA dated August 30, 2021.

111. Within days of the Citizen’s Petition filing, the greater scientific community had indeed begun a comprehensive review of Drs. Wang’s and Burns’s research and found *29 papers with red flags, as noted on PubPeer*. Nine of these flagged papers were co-authored by Dr. Burns and three were co-

authored by Dr. Steven E. Arnold, another scientist Cassava listed as a member of its Scientific Advisory Board.

112. The Citizen Petition authors, Drs. David S. Bredt and Geoffrey Pitt, later publicly revealed themselves in November 2021. The two scientists who, after uncovering Cassava’s wrongdoing, took out short positions on the Company’s stock were not typical short sellers, however, and neither worked for short seller firms. The petition’s first author, Dr. Bredt, is a neuroscientist with a degree in Chemistry from Princeton University and M.D. and Ph.D. degrees from Johns Hopkins University School of Medicine. From 1994 to 2004, Dr. Bredt served on the faculty of the University of California at San Francisco Medical School, attaining tenure as a Professor of Physiology.

113. More recently, from 2004 to 2011, Dr. Bredt worked for Eli Lilly and Company, first as Vice President of Integrative Biology and later as Vice President of Neuroscience Discovery and Early Development. And from March 2011 through March 2021, Dr. Bredt was the Global Head of Neuroscience Discovery for Janssen Pharmaceuticals. From 2017 to 2021, he also served as Site Head for Janssen’s La Jolla, California, site, which focused on research and development for neuroscience, immunology, and biotechnology. At both Janssen and Lilly, he oversaw research focused in part on Alzheimer’s disease.

114. Dr. Bredt’s research has yielded more than 225 papers that have been cited approximately 75,000 times in the scientific literature. His awards and honors include, among numerous others, the Society for Neuroscience Young Investigator Award, the Daniel H. Efron Award from the American College of Neuropsychopharmacology, the EJLB Neuroscience Research Fellowship Award, and the Klingenstein Fellowship Award in the Neurosciences. He has been awarded at least 10 NIH grants.

115. As discussed in a piece published in *The New Yorker*, the first time Dr. Bredt heard of Cassava ““was around February [2021], when there was this explosion in the stock price.”” He found it odd

that the stock was skyrocketing at that time on the basis of a trial without a placebo. You can't trust such results, he said, because it is simply "human nature to want things to work."

116. Dr. Bredt then started reading Cassava's research. He discovered that all the Company's publications associated with simufilam appeared to have been written by the same scientists: Drs. Wang and Burns. When Dr. Bredt consulted the papers, he was "shocked." "They were making statements that were incompatible with biology and with pharmacology," he told *The New Yorker*. If all the claims in these papers were true, Dr. Bredt said "they would win five Nobel Prizes."

117. He shared his concerns about Cassava with a friend and former medical-school classmate, Dr. Pitt, a cardiologist and a professor at Weill Cornell Medical College who conducts neuroscience research, who would become the second author behind the petition.

118. Dr. Pitt is the Ida and Theo Rossi Distinguished Professor of Medicine and Director of the Cardiovascular Research Institute at Weill Cornell Medicine with an Sc.M. degree from Johns Hopkins School of Public Health and M.D. and Ph.D. degrees from Johns Hopkins School of Medicine. Today, Dr. Pitt is a physician-scientist caring for patients with cardiovascular disorders and running a NIH-funded research laboratory studying the role of cellular electricity in the heart and brain. He has authored over 100 research papers in scientific journals including *Nature* and *Cell*, and has received numerous awards.

119. He previously held academic positions at Columbia University Medical School and Duke University Medical School before being recruited to Weill Cornell Medicine as the inaugural director of the Cardiovascular Research Institute. He has been a member of the Society for Neuroscience since 2001. During his career, Dr. Pitt has personally been awarded funding for more than 10 NIH grants and served on committees that review allegations of scientific misconduct at academic institutions and journals.

120. After examining Cassava's research, Dr. Pitt echoed Bredt's skepticism. As *The New Yorker* article explained, "It wasn't just that the science didn't make sense; there seemed to be signs of data manipulation." Together, Drs. Bredt and Pitt reviewed Cassava's pre-clinical research and the results the

Company presented on its clinical trials. Much of Cassava’s research involves Western-blot tests, a method used by scientists to detect and quantify specific protein molecules, which show up as dark bands on X-ray film. But Drs. Bredt and Pitt found that “some images of Cassava’s Western-blot tests looked off – as though they had been tweaked by a program such as Photoshop.”

121. Drs. Bredt and Pitt then honed in on Cassava’s decision to re-do its analysis of the May 2020 Phase 2b data. “Now, suddenly, it’s the best drug!” Dr. Pitt said, “That just doesn’t happen.” They further learned that Cassava had instituted a compensation scheme in which Barbier and other senior executives would be rewarded with cash bonuses if the Company’s stock maintained specific valuations for just 20 consecutive business days – incentivizing the Company and its executives to pump up the stock price.

122. As result, Drs. Bredt and Pitt sent Cassava’s papers to 10 prominent experts, including the neuroscientists: (i) Thomas Südhof, of Stanford University, who received the Nobel Prize in 2013; (ii) Roger Nicoll, of the University of California, San Francisco and; (iii) Don Cleveland, of the University of California, San Diego. Drs. Bredt and Pitt were struck by the fact that Cassava – despite claims about revolutionizing the treatment of Alzheimer’s – had gained little renown among specialists in the field. Dr. Bredt said, “The first question we asked was ‘Have you ever heard of Cassava Sciences?’ And every single one of them said no.”

123. When the scientists consulted Cassava’s research papers, ““the main reaction was “*Oh, my God, how could they get away with this?*””” Dr. Pitt said, adding, ““It appeared that someone had tried to crop” the Western blots in Cassava’s research “and cut out little pieces of one and put them in another.””

124. Dr. Südhof, in particular, said that the data in the papers ““looked suspicious and needed scrutiny,” and that the scientific conclusions were ‘unjustified.’” Südhof also “pointed out that there are a lot of scientific journals, and noted, ‘The fact that a paper is published in an apparently peer-reviewed journal doesn’t necessarily mean it was properly peer-reviewed.’”

125. Dr. Nicoll, who is an expert on the study of brain slices, told *The New Yorker* that “he was shocked to see Cassava assert that it had tested the effects of its drug on the brains of deceased Alzheimer’s patients which had been frozen and then thawed months, or even years, later.” “It’s hard for me to imagine how you could get any life from that tissue,’ he said. ‘I mean, this is wild. ***It’s zombie science!***”

126. In addition, as recently revealed in a July 21, 2022 article entitled “Blots on a Field? A neuroscience image sleuth finds signs of fabrication in scores of Alzheimer’s articles, threatening a reigning theory of the disease” in the journal *Science*, the conclusions in the Citizen Petition were further supported by Dr. Matthew Schrag, a neuroscientist and physician at Vanderbilt University, who reviewed Drs. Burns’s and Wang’s articles as consultant to the Citizen Petition’s authors. Dr. Schrag, however, did not participate in short selling Cassava’s stock. As part of this work, Dr. Schrag identified dozens of apparent duplications and manipulations, many of which were reported in the Citizen Petition. Dr. Schrag explained in the article that his concern is that Cassava’s research may slow the race to find effective treatments for the neurodegenerative disease.<sup>1</sup>

127. As *Science* reported, the independent image analysts and Alzheimer’s experts who reviewed Dr. Schrag’s findings at the journal’s request “generally agree with him.” Charles Piller, the award winning author of the *Science* article, Tweeted the day the article was published, “I vetted Schrag’s findings with numerous top Alzheimer’s experts, plus forensic image specialists. Many were ***stunned by the apparent extreme manipulations*** in” Cassava-linked cases.

128. Indeed, as Dr. Bredt concluded in *The New Yorker* article, “In my thirty-five years of research, ***I’ve never seen such a long trail of apparently clear misrepresented scientific data.***”

129. The United States Department of Health and Human Services’ Office of Research Integrity (“ORI”), however, has recognized for years that Western blot manipulation presents a serious problem for

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<sup>1</sup> In fact, per *Science*, Dr. Schrag’s investigation uncovered that the entire theory on which Cassava’s treatment is based, that amyloid  $\beta$  is a primary cause of Alzheimer’s disease, may itself be based on fabricated and manipulated research by other scientists.

the integrity of biomedical research. An article in the ORI's Spring 2018 News Letter stated that "widespread and easy access to digital image processing software, such as Photoshop, has increased the odds of manipulated images appearing in all types of publications, including scientific journals," and called out Western blots as an example of images subject to manipulation.

130. Under the regulations that implement ORI's statutory authority, 42 C.F.R. Part 93, research misconduct is defined as "fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results." As such, "intentional manipulation of images to mislead readers or misrepresent research results is research misconduct," according to the ORI newsletter. Drs. Bredt and Pitt had uncovered widespread research misconduct by Cassava's two principal scientists.

#### **F. Independent Experts Corroborate the Citizen Petition**

131. In the wake of the Citizen Petition, few, if any, independent experts in the field have stepped up to publicly support Cassava. Instead, more and more have spoken out against the Company.

##### **1. Dr. Elisabeth Bik Corroborates the Allegations Days after they are Made**

132. Dr. Elisabeth Bik is an expert in identifying improper duplication and manipulation in published biomedical images from scientific experiments. She has a Ph.D. in microbiology and spent 15 years studying the microbiome at Stanford University. In 2019, she launched a blog called Science Integrity Digest and dedicated herself to reviewing scientific images as her full time career. According to a June 23, 2021 profile on Dr. Bik in *The New Yorker* entitled "How a Sharp-Eyed Scientist Became Biology's Image Detective," she had, at the time of publication, identified more than 4,900 articles containing suspect image duplications in just six and a half years. She has since identified many more, including those concerning Cassava.

133. Dr. Bik's work has been studied by Ferric Fang and Arturo Casadevall, two prominent microbiologists and the respective editors-in-chief for the scientific journals *Infection and Immunity* and *mBio*. In 2016, *mBio* published the results of this review. The team concluded that out of the tens of



thousands of studies Dr. Bik reviewed, her determination was right **90% of the time**, and the remaining 10% of images included some that were too low-resolution to allow for a clear answer.

134. Renee Hoch, an editor for the journal *PLOS One*, told journalists at *The New Yorker* that of the first 190 or so of Dr. Bik's cases that the journal had resolved, 46% required corrections, around 43% were retracted, and another 9% received "'expressions of concern.'" In **only two** of the resolved papers was nothing amiss. "'In the **vast majority** of cases, when she raises an issue and we look into it, we agree with her assessment,'" Hoch said.

135. On August 27, 2021, Dr. Bik posted an entry on Science Integrity Digest, entitled "Cassava Sciences: Of stock and blots." She reported that "I took a look at the problematic photos included in the [Citizen Petition] report, and **agree with most of those concerns**." She "also found some additional problems," too, after reviewing "[o]ther papers with image concerns," stating:

At least five other articles from the Wang lab at CUNY appear to show image concerns as well. These papers might not be directly related to Simufilam research, but they are still indirectly connected to Cassava Sciences or its drug candidates. Some articles are also about Alzheimer's Disease or filamin A binding; some were funded by Pain Therapeutics, the Cassava Sciences precursor; and some are authored by Lindsay H Burns, the current Senior VP Neuroscience and lead scientist of Cassava Sciences. And of course, as mentioned above, Dr. Wang is one of Cassava's Scientific Advisors. Together, the problems in these additional articles raise concerns about Western blots and perhaps also other data from this lab spanning a period of 15 years.

136. In her post, Dr. Bik made it clear she had no conflicts of interest, writing "I do not own any Cassava Sciences shorts or stock, . . . [n]or stock from other pharmaceutical companies that might be working on competing drugs" and that "I was not paid by any person or organization to investigate these allegations, to analyze these papers, or to write this post."

137. Dr. Bik later told *The New Yorker* that she had asked Dr. Wang's lab at CUNY to provide high resolution versions of the original Western blots, **but neither Dr. Wang nor Cassava would provide them**, and "'the silence of the lab,' as she put it, had intensified her skepticism." Dr. Bik also told *The New York Times* for an April 18, 2022 article on Cassava that the problematic images she highlighted from the



Citizen Petition along with the additional problematic images she uncovered that appear to show that Cassava’s results had been copied and pasted from other experiments “‘were of *severe concern*,’” and that “[b]ased on the *pattern of irregularities* in images in multiple papers, she believes ‘it is *highly likely* that there was some manipulation going on.’”

138. After having followed the allegations in the Citizen Petition for months and having extensively researched Cassava’s scientific papers, Dr. Bik concluded on Twitter that “[b]ased on my due diligence, I will *never* invest in Cassava Sciences.”

## 2. Expert Image Analysis Further Confirms the Citizen Petition’s Findings

139. An expert retained by Plaintiffs’ counsel, Dr. Mike Rossner, Ph.D., reviewed the image manipulation allegations raised by the Citizen Petition in nine published research articles related to Cassava that formed part of the pre-clinical scientific basis for the clinical trials in simufilam and one Cassava scientific poster presenting clinical results from the Company’s Phase 2b trial. Dr. Rossner is an expert in analyzing biomedical images for data manipulation. He previously served as the Managing Editor of *The Journal of Cell Biology* from 1997 to 2007 and as Executive Director of The Rockefeller University Press from 2006 to 2013, where he was involved in handling hundreds of cases of suspected image manipulation and spearheading new policies to screen for image manipulation. He has published numerous articles on the guidelines for handling suspected image manipulation, including “What’s in a picture? The temptation of image manipulation.” In 2009, Dr. Rossner was awarded the SPARC Innovator Award for his efforts to promote data integrity and public access to scholarly research. He has degrees in molecular biology from Princeton University and the University of Edinburgh.

140. Dr. Rossner found with high confidence and to *a reasonable degree of scientific and technical certainty* that numerous of the Citizen Petition’s data manipulation allegations are correct. Thus, the published data that are the subjects of those allegations (and the conclusions drawn from them) are unreliable. For 11 more allegations, Dr. Rossner found they raised sufficient concerns about the integrity of

the data to warrant further investigation by examining the source data underlying the relevant published figures. In total, Dr. Rossner concluded that 19 instances of alleged manipulation, duplication or misrepresentation that he reviewed *have merit* and have the potential to change the interpretation of the data in such a way that supports the authors' conclusions. Dr. Rossner's analysis, notably, was not exhaustive and is likely only the tip of the iceberg.

141. Moreover, many of the alleged manipulations or duplications *have the hallmarks of deliberate actions* using image-processing software, and, thus, do not appear to be the results of inadvertent error on the part of the authors. As Dr. David Vaux, the Deputy Director of Science Integrity and Ethics at the Australian Walter and Eliza Hall Institute of Medical Research stated on the science news website *Retraction Watch* after the Citizen Petition surfaced: "It is *not conceivable* that features in the images (such as apparent duplications) arose due to coincidence (chance) or accident, leaving the only plausible explanation being that the images were *deliberately* falsified or fabricated."

142. The findings of the Citizen Petition and a review of those findings by Drs. Bik and Rossner, who, among others, have independently validated the Citizen Petition, are alleged in further detail below.

### **G. The Citizen Petition's Substantive Findings**

143. The Citizen Petition raised specific problems with the quality and integrity of the laboratory-based pre-clinical studies surrounding simufilam and Cassava's clinical trial results.

#### **a. Integrity of Western Blot Data**

144. Many experiments in the work by Drs. Wang and Burns involve Western blotting. Using this technique, proteins from tissue samples are separated on "gels" in a series of vertical lanes; the proteins are then transferred to a paper-like membrane, and antibodies are used to detect specific proteins on the membrane, producing an image of specific proteins or "bands." Each band generally has a slightly different shape. As noted in an article posted on *Retraction Watch*, "In Western blots, every band has their own characteristics, they're like faces."

145. Various types of Western blot manipulation and duplication exist, including by splicing. Western blot images rarely have sharp edges in them. The protein bands are amorphous shapes by the very nature of the polyacrylamide gel matrix used to separate them. Thus, when sharp lines are visible in a blot image, it is a clue that the image may have been spliced. Splices in blot images can indicate various types of image manipulation. Vertical splice lines on both sides of a lane (or both sides of a collection of lanes) can indicate that the lane (or collection of lanes) was copied or cut from another location in the image – or from another image – and pasted in. A visible splice line is produced because of differing background pixel patterns or intensities between the newly juxtaposed regions.

146. The Citizen Petition found that Drs. Wang, Burns and Cassava misrepresented the Company’s pre-clinical and clinical research results for more than 15 years in public disclosures and published manuscripts. The initial examination of their published Western blots in the Citizen Petition “identified many dozens of examples of protein bands that appear to have been duplicated and/or misrepresented, a Western blot that was used twice to represent different experimental conditions, and a normalization blot that appears to have been manually constructed. [In addition,] [s]ome bands appear to have been ‘reused’ in papers concerning different research topics that were published five years apart.”

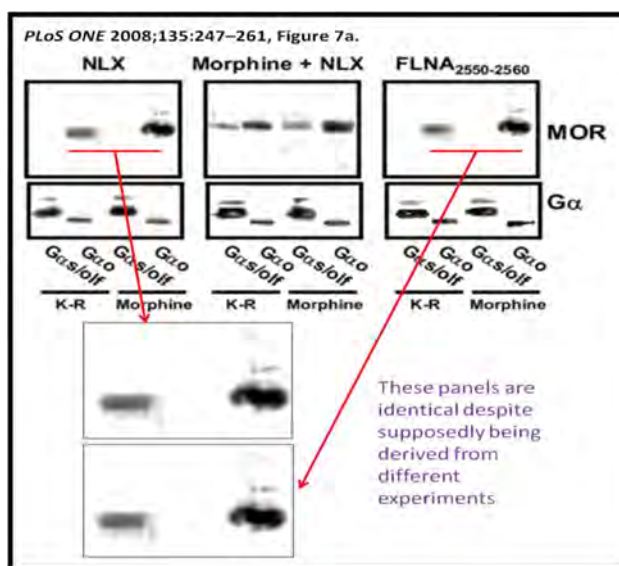
147. The Citizen Petition’s analysis of Drs. Wang’s and Burns’s published journal manuscripts thus shows a series of anomalies that suggest a 15-year *pattern of systematic data manipulation* and misrepresentation in *virtually every publication* underlying Cassava’s simuflam claims.

#### (1) Manipulations in Foundational Cassava Pre-Clinical Studies

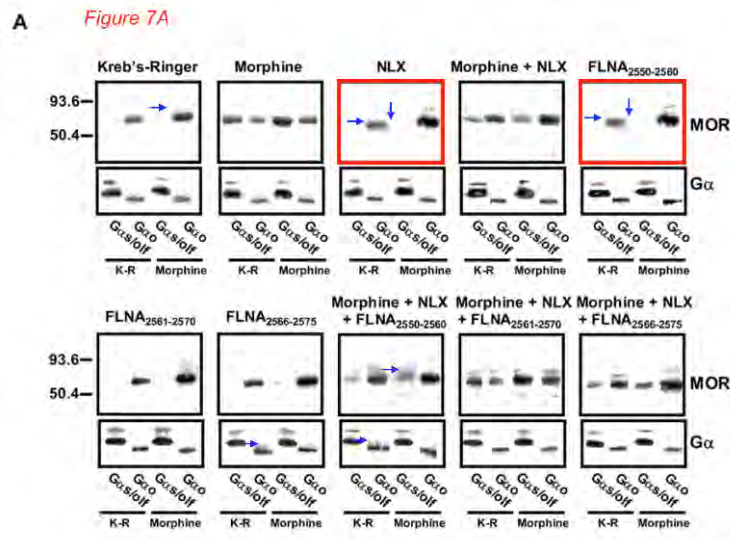
148. The Citizen Petition identified numerous instances of manipulations, which have been corroborated by independent experts, in key Cassava pre-clinical research foundational to the continued commercial development of simuflam.

(i) **Reused/Misrepresented Western Blot; *PLoS ONE* 2008 [Figure 7A]**

149. The Citizen Petition found that Drs. Burns and Wang presented “a series of overexposed and selectively cropped gels that appear to show spliced experiments (*i.e.*, two separate experiments combined as if they were done simultaneously)” in their 2008 paper “High-Affinity Naloxone Binding to Filamin A Prevents Mu Opioid Receptor–Gs Coupling Underlying Opioid Tolerance and Dependence,” published in *PLOS ONE*, which was funded by Pain Therapeutics and forms part of the foundational research on which the commercial development of simufilam is based. Signs suggesting such splicing include “the sharp upper and right border for the band in the Gαo lane.” Further, “**Figure 7A** of that paper (below) appears to show two IDENTICAL panels (red arrows) for what are reported as different experiments.” According to the Citizen Petition, “the similarity in these images *could not have occurred by chance.*”

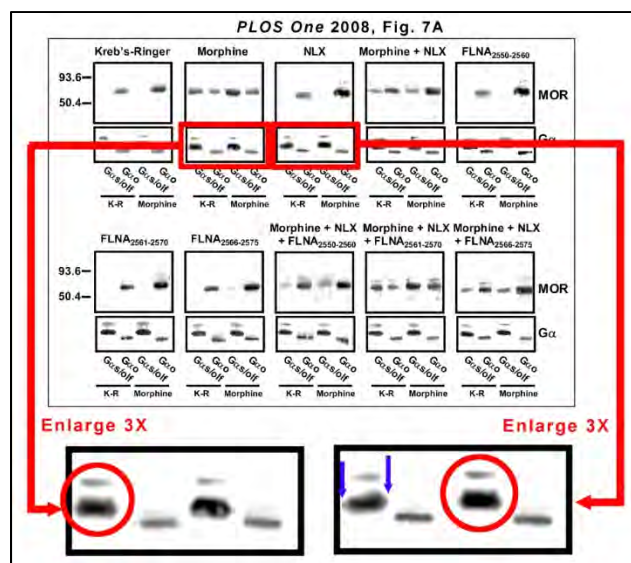


150. Dr. Bik agreed. In her August 27, 2021 post in Science Integrity Digest, “Cassava Sciences: Of stock and blots,” Dr. Bik wrote that **Figure 7A** “contains two blots that appear to look *identical* [in red boxes, below]. In addition, some sharp background transitions suggestive of splicing may be visible [indicated by blue arrows].”



151. Dr. Rossner also agreed, finding with high confidence that based on similar band shapes, sizes, internal intensity variations, edge elements, background elements, relative positions and positions relative to background elements, *the two image panels are duplicates derived from the same source image*. As a result, the panels cannot depict samples subjected to different treatments as claimed in the figure, and the controls are unreliable.

152. Further, Dr. Rossner found additional duplication and manipulations in **Figure 7A**. Specifically, Dr. Rossner found, with high confidence, that: (i) based on similar band shapes, sizes, orientations, internal intensity variations, edge elements and relative positions, that the bands highlighted in the red circles (below) are *duplicates derived from the same blot*; and (ii) that the lower band in lane one in the right-hand panel indicated with blue arrows (below) has splice lines on either side of it and that *it is apparent that the image has been altered from the original*.



153. In addition to data manipulation, the Citizen Petition also questioned the plausibility of the high affinity binding between Naloxone and Filamin A reported in the paper, noting that **Figure 3** claims that Naloxone [3H]NLX binds with “low picomolar affinity to Filamin A,” but that “it is puzzling why previous studies have not reported picomolar binding affinity for naloxone in [the] brain.”

154. Notably, on March 30, 2022 the journal *retracted* this entire paper, and an additional paper authored by Drs. Wang and Burns, based, in part, on the data manipulations raised in the Citizen Petition.

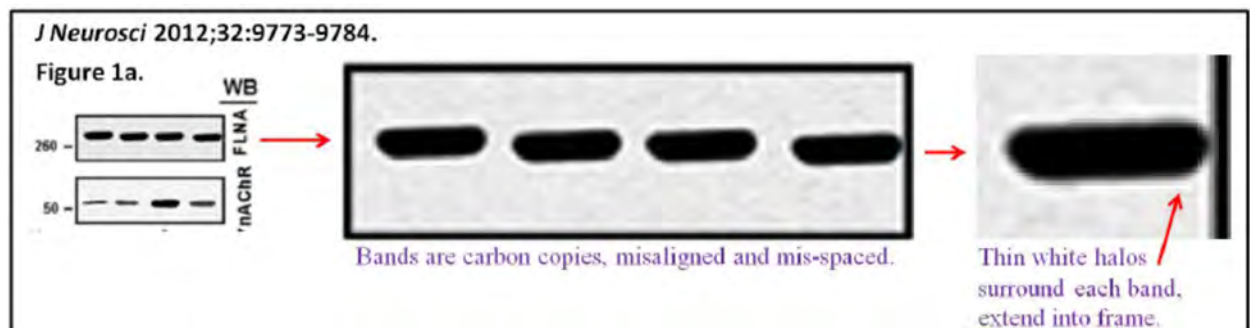
(ii) **Duplicated Western Blots; *Journal of Neuroscience*, 2012 [Figures 1A, 6B, 8A, 8B, 9A, 11A, 12A]**

155. Next, the Citizen Petition found that “[t]he *foundational* paper from Drs. Wang and Burns that links Filamin A and PTI-125 to Alzheimer’s disease,” the 2012 *Journal of Neuroscience* paper “Reducing amyloid-related Alzheimer’s disease pathogenesis by a small molecule targeting filamin A,” which was funded by Pain Therapeutics, “appears to contain a collection of questionable western blots” where “the authors appear to have *duplicated and transposed bands*.”

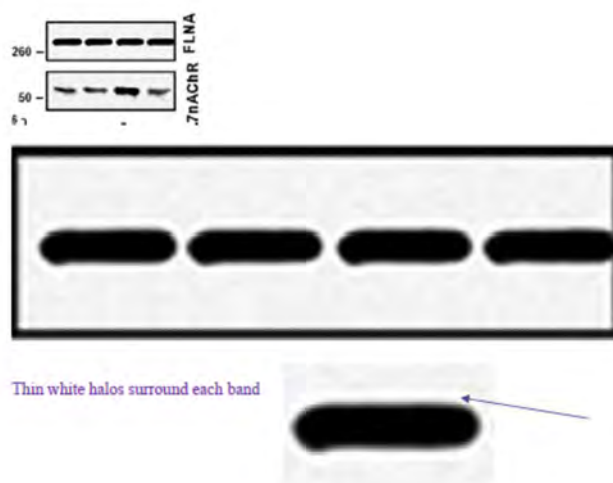
156. After reviewing the Citizen Petition, Dr. Bik wrote in her August 27, 2021 blog post, “[a]ccording to the [Citizen Petition] report, several Western blots in the 2012 *J Neurosci* paper – in

particular those with control proteins – show oversaturated bands with little background detail, irregularly spaced bands, and bands that look remarkably similar. *I agree with these concerns . . .*”

157. First, according to the petition, in **Figure 1A** (below), “the four Filamin A bands in the top set are more similar to each than can be expected by chance and appear to be duplicates. The images at right are magnified, showing that the pixels containing the bands are *essentially identical*.” Moreover, there are “thin white halos surrounding each band,” which is “most common when components from multiple images are combined *using photo editing software*.”



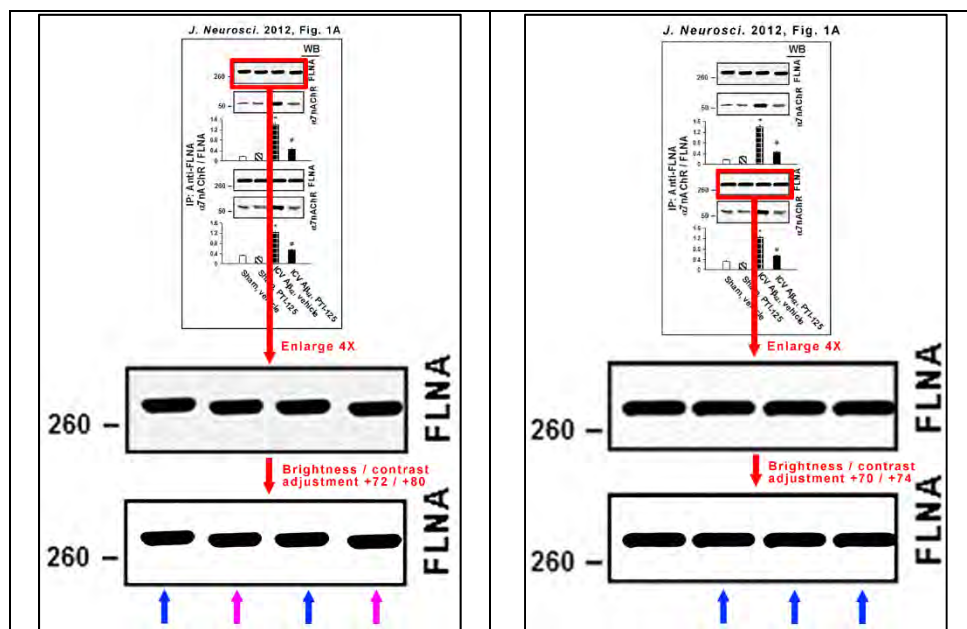
158. In addition, the Citizen Petition found that the “four Filamin A bands in the bottom set of **Figure 1A** [below] appear to be identical to each other. This degree of similarity is unlikely to occur by chance, and the thin white borders surrounding each band could be due to merging multiple images in a photo editing software.”





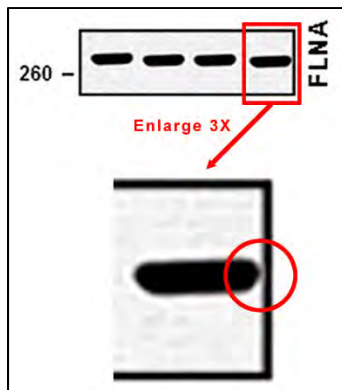
159. Dr. Bik concurred on PubPeer that the bands in the FLNA blots of **Figure 1A** “appear over-saturated, similar in shape, and irregularly spaced.”

160. Dr. Rossner further agreed that the similarities in the top and bottom panels, reflected in the two analysis images below, *render the data questionable*.



161. In addition, Dr. Rossner found that the right-hand band in the top FLNA panel appears to be placed on top of the black frame in **Figure 1A**. The overlap suggests that the band was copied and pasted onto an image background, which had already been surrounded with a black border. *See below.* This would explain how the image of the band ended up on top of the border. If the border had been placed around an unmanipulated, cropped, Western blot image, it would appear on top of the band, not behind it. Accordingly, Dr. Rossner found this anomaly provides additional evidence that this image panel was *falsified by duplicating individual bands using image-processing software*.



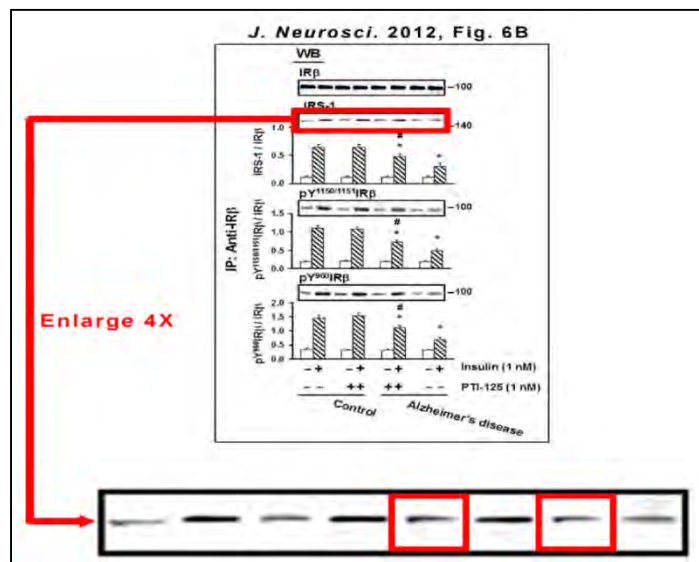


162. Second, according to the Citizen Petition, in **Figure 6B** (below), the “four rightmost bands appear to be identical to each other. This degree of similarity is *unlikely to occur by chance*.”

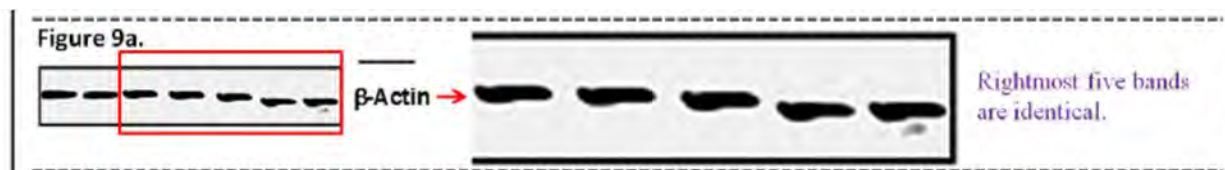


163. Dr. Bik agreed on PubPeer that in **Figure 6B**, “the IRb bands (top blots) appear to be irregularly spaced, and several bands are very similar in shape.”

164. Dr. Rossner also found that these similarities render the data questionable. In addition, Dr. Rossner found similarities in another apparent duplication in a panel in **Figure 6B** (below).

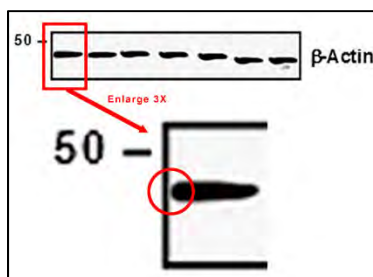


165. *Third*, according to the Citizen Petition, “[t]he five rightmost actin bands” in **Figure 9A** (below) “have a distinctive shape, but are nevertheless identical to each other. That these bands all have apparently *identical* ‘dipper’ shapes *cannot occur by chance*.” And “[a]s above, the thin white border surrounding each band is prominently seen again.”

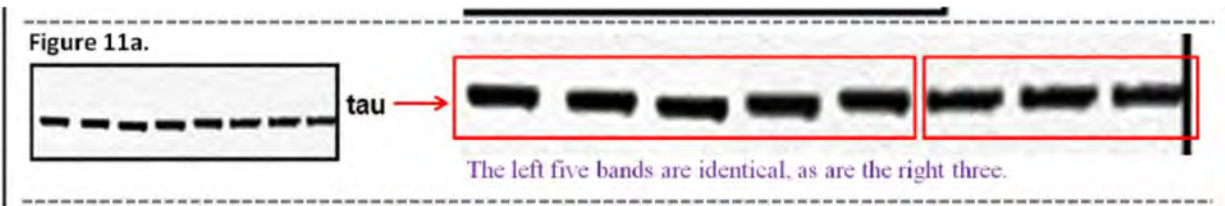


166. Dr. Bik also found these five bands in the β-Actin blot to “look remarkably similar.” And Dr. Rossner likewise concluded that the similarities render the data questionable.

167. In addition, Dr. Rossner found that the left-hand band in the β-Actin panel appears to be placed on top of the black frame in **Figure 9A** (below). The overlap again suggests that the band was copied and pasted onto an image background, which had already been surrounded with a black border. If the border had been placed on an unmanipulated, cropped, Western blot image, it would appear on top of the band, not behind it. This anomaly thus provides *additional evidence that this image panel was falsified by duplicating individual bands using image-processing software*.

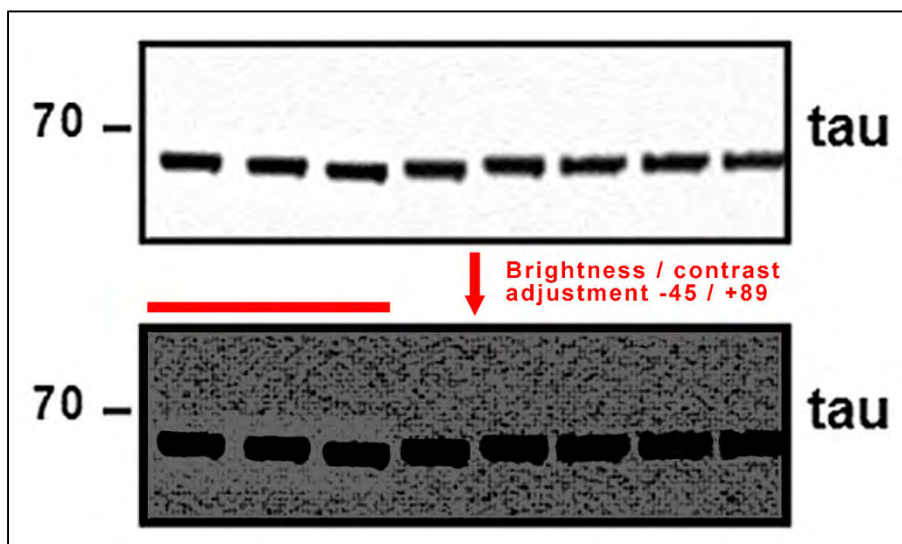


168. *Fourth*, the Citizen Petition found that, in **Figure 11A** (below), the “five leftmost tau bands appear to be *identical* to each other, AND the 3 rightmost tau bands appear to be identical to each other. These degrees of similarity are *unlikely occur by chance*.”

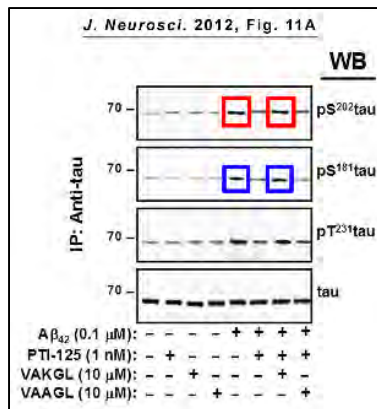


169. Dr. Bik agreed that those blots “look very similar to each other,” and Dr. Rossner also concluded that similarities in the panel render the data questionable.

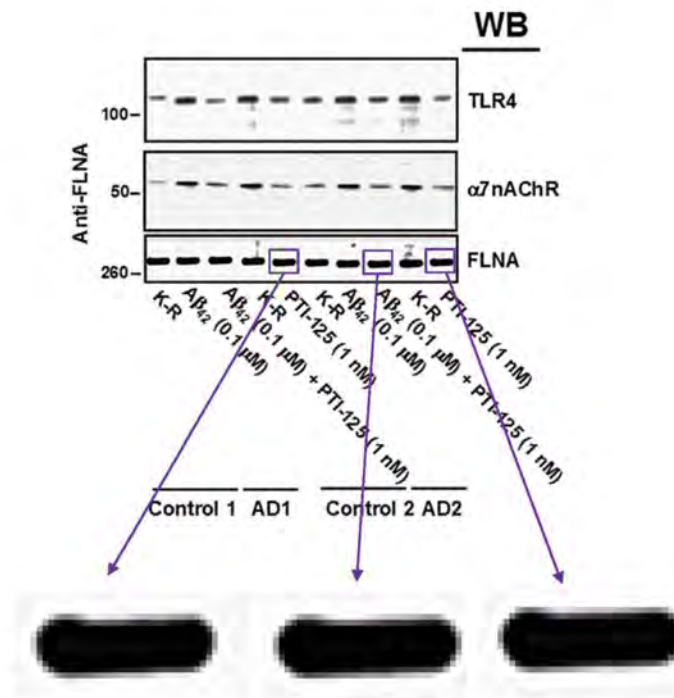
170. In addition, Dr. Rossner found an inconsistent background in the total tau panel of **Figure 11A** (below). This type of background inconsistency can occur if the intensity of pixels in this particular region was altered when the surrounding pixels were not. As a result, Dr. Rossner is highly confident that the image was *altered in some way, as this is highly unlikely to occur naturally*.



171. And further, Dr. Rossner found additional apparently duplicated bands in **Figure 11A** (below), not mentioned in the Citizen Petition, rendering this data questionable, as well.

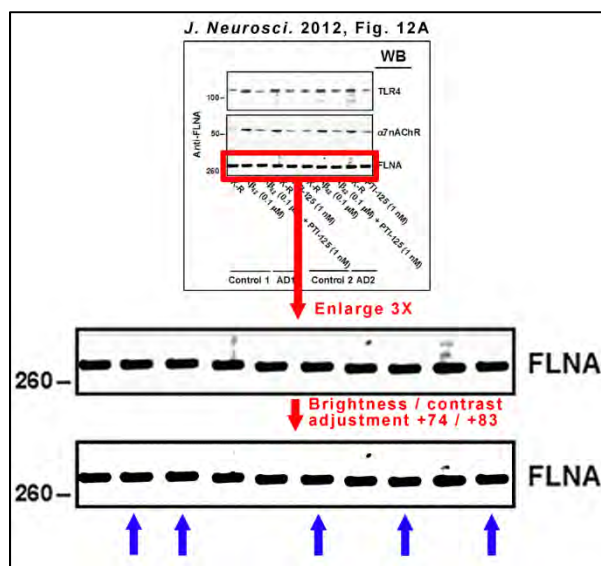


172. Fifth, the Citizen Petition found that, in **Figure 12A** (below), “[t]he ten filamin A (FLNA) bands appear *identical* in size and shape. As protein bands on Western blots typically have unique features, ten consecutive indistinguishable bands are *exceedingly unlikely* to occur by chance and were *probably manually duplicated*.”

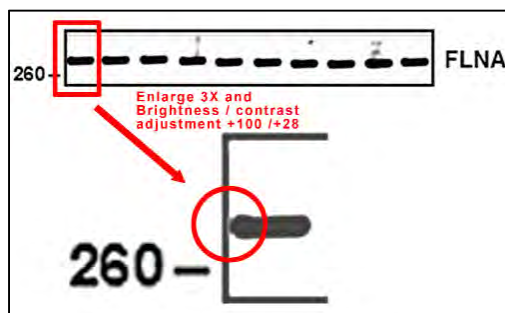


All ten virtually indistinguishable FLNA bands are exactly 11 pixels high and 32 pixels wide. Three examples are magnified here for illustration.

173. After review of **Figure 12A**, Dr. Rossner also found that the bands indicated with the blue arrows have similarities (below) that render the data questionable.

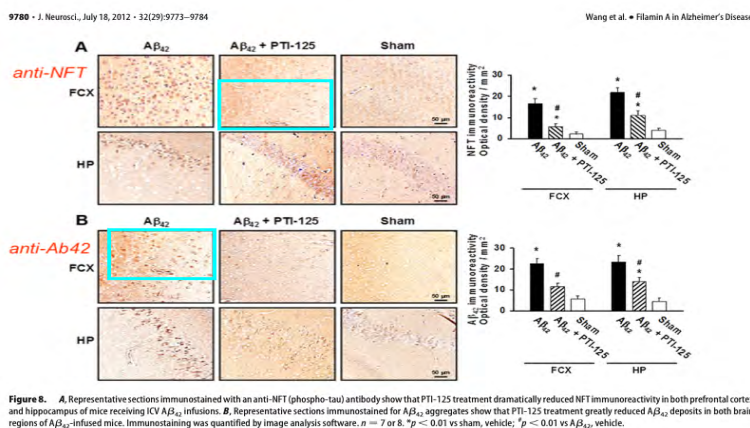


174. In addition, Dr. Rossner identified that the left-hand band in the FLNA panel appears to be placed on top of the black frame in **Figure 12A** (below). Again, the overlap suggests that the band was copied and pasted onto an image background, which had already been surrounded with a black border. If the border had been placed on an unmanipulated, cropped, Western blot image, it would appear on top of the band, not behind it. Thus, this anomaly provides additional evidence that this image panel was *falsified by duplicating individual bands using image-processing software*.



175. *Sixth*, Dr. Bik identified another concern, not mentioned in the Citizen Petition – an additional potential duplication between two panels in **Figure 8** (below). Dr. Bik wrote on her blog that “[t]wo panels displaying different immunostaining and treatment appear to share an area that looks similar

... indicated below with cyan boxes,” and that these “might be two consecutive tissue sections, perhaps stained for different proteins, although some features are remarkably similar in the right hand of the image.” She concluded, “the images are representing differently treated mice, so the samples should not look so similar.”



176. As Drs. Bredt and Pitt explained in their petition, “[i]ndividually, each of these examples is concerning, but *together they form a pattern that strongly calls into question the integrity of this publication* (and the other publications from these authors with similar patterns of band insertion).” This is especially significant because “[t]he work in question here serves *as THE foundational research linking PTI-125 (Simufilam) to Alzheimer’s disease.*”

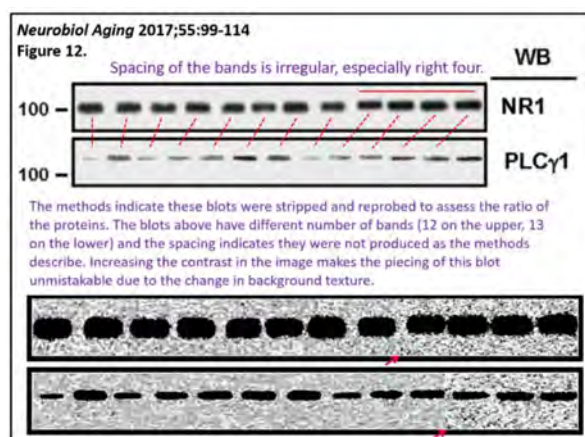
177. Due to these allegations, the *Journal of Neuroscience* issued an Expression of Concern on this paper on December 17, 2021, as further detailed in ¶¶33; 357-360 below, a highly atypical step indicating that the editors have reason to question the integrity and accuracy of the paper.

(iii) **Manipulation in Data from *Neurobiology of Aging*, 2017; [Figures 12, 8B, 3B, 6, 7]**

178. The Citizen Petition identified that **Figure 12** in Drs. Wang’s and Burns’s 2017 paper in *Neurobiology of Aging*, “PTI-125 Binds and Reverses an Altered Conformation of Filamin A to Reduce Alzheimer’s Disease Pathogenesis,” another foundational paper funded by Pain Therapeutics, includes a NR1 blot that contains 12 bands whereas all the other blots in this figure contain 13 bands (below), despite



the fact that the process used to analyze these bands does not introduce or remove band lanes. Also, the NR1 bands show different spacing than the bands in the PLC $\gamma$ 1 blot, which, according to the Citizen Petition, strongly suggests that the NR1 and PLC $\gamma$ 1 Western blots could not have derived from the same gel.



179. Dr. Rossner agreed that the top panel contains 12 lanes and the bottom panel contains 13 lanes, and that all of the rest of the experimental panels in this figure contain 13 lanes. Thus, the NR1 panel is *not a valid immunoprecipitation control* for any of the experimental panels, and the conclusion that PTI-125 increased the association of N-methyl-D-aspartate receptor with six different signaling molecules is *unreliable*.

180. Another “major problem” the Citizen Petition identified with the 12-band blot is that the spacing of the bands is irregular, particularly on the right half (lanes 7-12). According to the petition, “[t]his asymmetry in band spacing is incompatible with the regular shape of the combs used for gel loading. Therefore, the 12-band blot was *almost certainly* pasted together from different sources.”

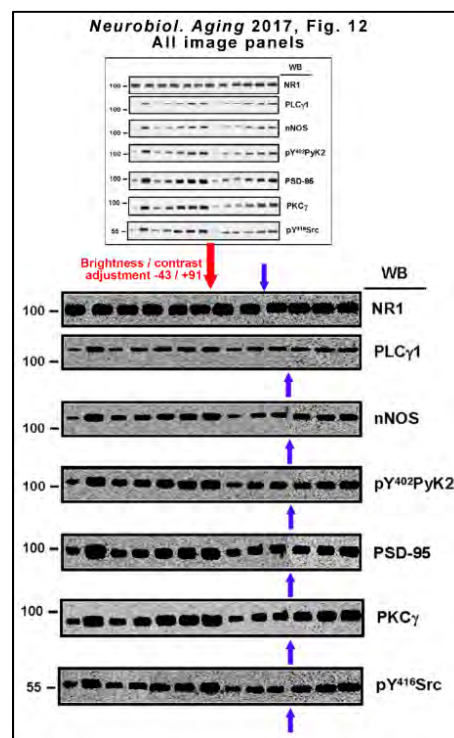
181. Further evidence that the bands derive from different sources cobbled together is apparent when the contrast of the image is adjusted. As revealed in the Citizen Petition, “the magnified panels in the figure [above], in the NR1 (top row) there is a sharp contrast between the background for the leftmost 8 bands and the background for the rightmost 4 bands, marked with a red arrow. In the magnified panel for

PLC $\gamma$ 1 (bottom row), there is also evidence of splicing. Again, the red arrow denotes a sharp background contrast between the leftmost 9 bands and the rightmost 3 bands.”

182. Dr. Bik wrote in her August 27, 2021 post that she “agree[ed] with this concern.”

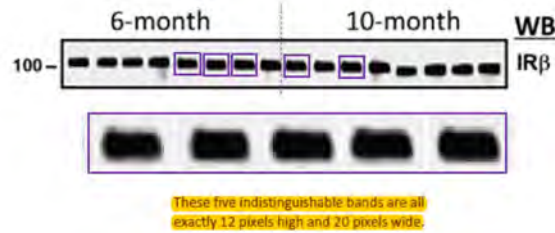
183. Dr. Rossner also agreed, finding, with high confidence, that based on the inconsistencies between the backgrounds on either side of each of the splice lines and sharp lines of demarcation the image panels were spliced at the indicated locations.

184. In addition, Dr. Rossner found that *all* of the image panels in **Figure 12** appear to be spliced. The blue arrows (below) indicate splice lines in all of the image panels.

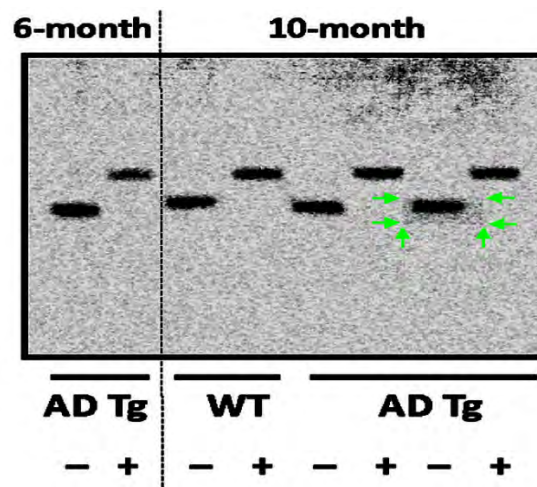


185. The Citizen Petition appendix also identified “many examples” of “manipulated and cropped Western blots” in **Figure 8B** (below), which contains Western blots from mice treated with PTI-125. According to the petition, “[t]he top blot displays a western blot using an antibody for IR $\beta$  (see label on the right). The similarity in size and shape of the bands in the purple boxes seemingly could not have occurred by chance. This and many other blots in this paper appear to have been manipulated.”

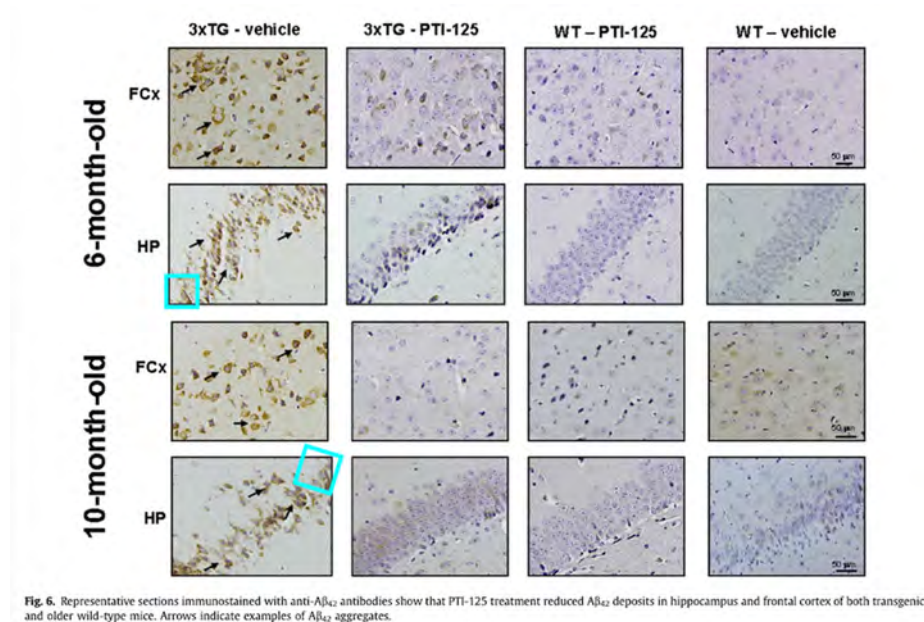




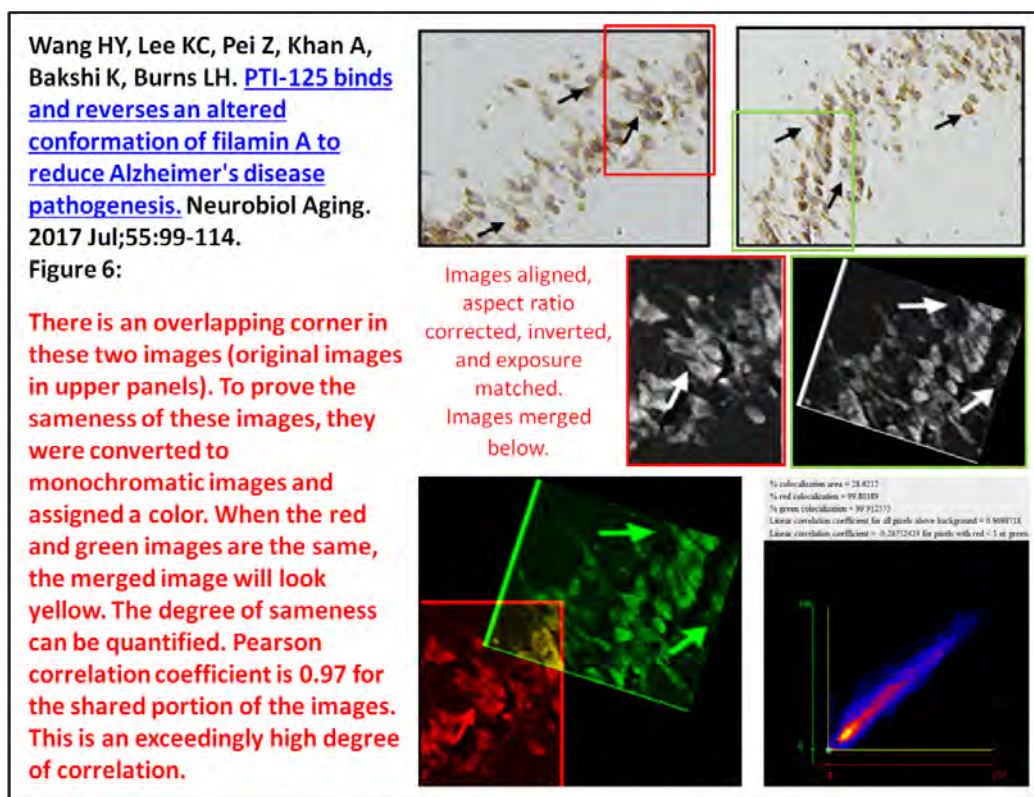
186. And Dr. Bik detailed in her August 27, 2021 blog post, “[a]n additional finding by me – not mentioned in the [Citizen Petition] report” is the “presence of a dark rectangle around [the] band” in **Figure 3B** (below). Dr. Bik stated: “This could mean that the band shown in that lane may have been derived from another blot, marking it hard to know exposure or size of the band relative to the other bands in that photo.”



187. Upon further review, Dr. Bik later identified another apparent duplication in **Figure 6** not mentioned in the Citizen Petition in an October 2021 posting on PubPeer. She noted that “[c]yan boxes highlight an area that appears to be visible both in the 6 month old HP panel as well as the 10 month old HP panel, albeit rotated and perhaps distorted.”



188. Another commenter on PubPeer also reviewed the same image and another in **Figure 7** using image analysis tools to make Dr. Bik's concerns "harder to dismiss." The commenter found "[i]n each of the apparently duplicated images, the images are rotated and stretched with changed contrast settings, which make it harder to detect the apparent duplications," *a deliberate act*, and provided an analysis (below) that "quantitatively assesses the sameness of the images."

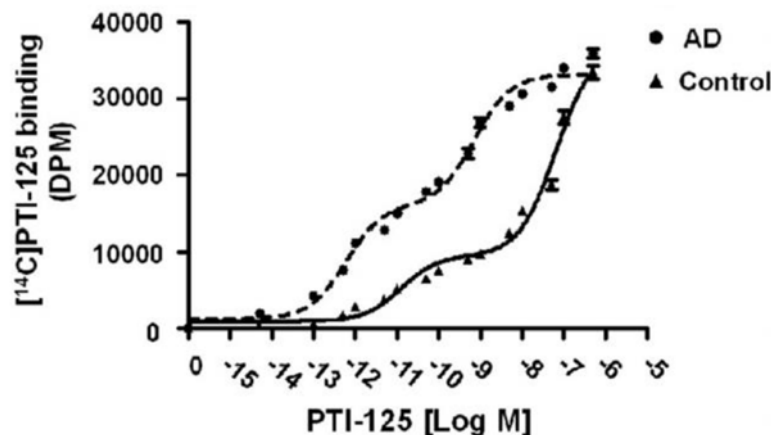


189. Due to allegations of data manipulation, the journal later issued an Expression of Concern on this paper on March 22, 2022, as further detailed in ¶¶414-418 below, indicating that the editors have reason to question the integrity and accuracy of the paper.

190. In addition to identifying instances of data manipulation and duplication, the Citizen Petition also found scientifically implausible results from Cassava's experiments in this paper, discussed below, further calling into question the integrity of their claims. According to the Citizen Petition, these aspects of Drs. Wang's and Burns's research are incompatible with scientific norms, and thus further support the petition's conclusions that the data underlying Cassava's clinical and pre-clinical studies was improperly manipulated.

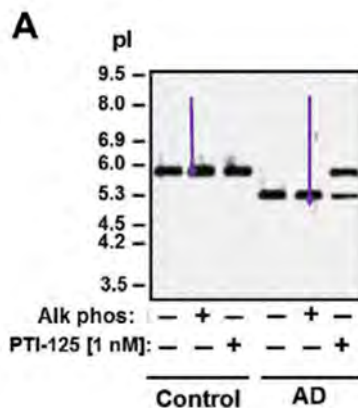
191. **Remarkably High Affinity Binding Between PTI-125 and Filamin A, Figure 1B.** First, fundamental to simuflam's activity in Alzheimer's disease is Cassava's claim that simuflam potently binds to filamin A. Evidence for this is unique to Drs. Wang and Burns and Cassava, and is presented in **Figure 1B**. Yet, no other direct binding studies between PTI-125 and filamin A have been

reported. **Figure 1B** claims that PTI-125 has femtomolar binding affinity for filamin A in the Alzheimer's disease, but, as the Citizen Petition states, "[t]here is scant precedent for a small molecule to bind so potently to a cytoskeletal protein. The claimed affinity seems higher than that of any other small molecule binding to any cytoskeletal protein. Figure 1B in this paper also shows that PTI-125 displacement occurs over 7 orders of magnitude. This 'shallow' displacement is *highly unusual/unprecedented*. An experienced pharmacologist could advise that this is suspicious / implausible."



192. **100% of Filamin in Altered Conformation in Alzheimer's Disease and Largely Restored to Correct Conformation by PTI-125.** *Second*, **Figure 2A** (below) presents a gel showing that Filamin A isoelectric point shifts from 5.9 in control to 5.3 in Alzheimer's disease (purple arrows for lanes 1 and 4). The Citizen Petition reported that "[t]his is suspicious for two reasons":

First, Alzheimer's disease affects only a small subset of neurons in a diseased brain, so it is scientifically unclear how 100% of Filamin A could shift. Second, isoelectric focusing gels do not typically "look" like the image below. Especially for a 290 kD protein like Filamin A, one would not expect such crisp bands in isoelectric focusing. An experienced biochemist could advise that this figure is suspicious / implausible. This is especially suspect considering the apparent pattern of band manipulation by Drs. Wang and Burns on Western blots. Similar experiments are shown in other publications.



193. **PTI-125/Simufilam Improves Memory in Mouse Model of Alzheimer’s Disease.**

Third, **Figure 9** shows a pre-clinical study of simufilam in a mouse model of Alzheimer’s disease and misinterprets the data as showing “improvements in memory.” The Citizen Petition concluded that “[i]t is dubious that any legitimate experiment approximating the methodology described could yield the reported result.” For instance, the paper shows data from a Y-maze which is used to assess memory in mice. Animals are placed in an apparatus made of three tubes which interlock in the middle, similar to a Mercedes Benz emblem.

194. After a mouse explores one arm of the Y-maze and returns to the center, they must decide which of the other two tubes to enter next. A normal mouse will generally avoid the tube that was most recently explored resulting in a pattern where they spontaneously alternate between each of the tubes. According to the Citizen Petition, “[n]ormal mice would be expected to follow this pattern 70-80% of the time as a rough estimate. If a mouse has memory impairment, the selection of which tube to enter will be random, and the alternation rate should be about 50%. Remarkably, wild type mice and transgenic mice in Wang’s study spontaneously alternated less than 20% of the time, which is an atypical result. Drug treatment in 6 month old transgenic mice, increased the rate of alternation to over 30%.”

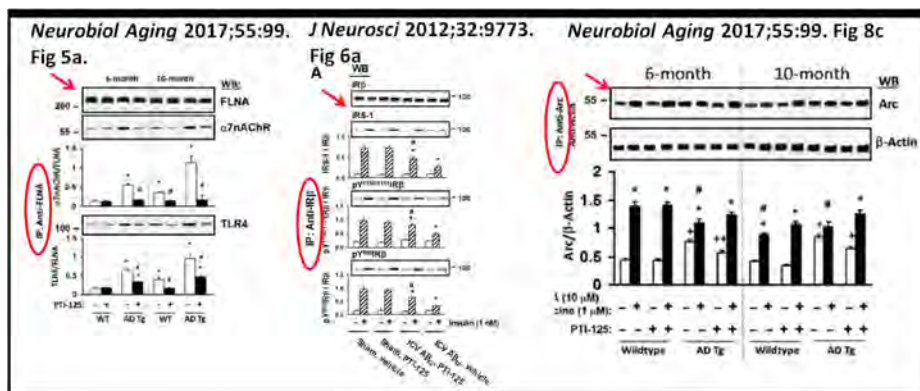
195. The petition concluded that “[t]his raises a number of issues: (1) this pattern of results is unlikely to occur and suggests, at the least, the experiment was conducted incorrectly, and (2) if the result



were legitimate, the drug treatment changing the mice's behavior to closer to 50% spontaneous alternation (*i.e.*, closer to random) would be more accurately interpreted as evidence of *worse* memory performance.” (emphasis in original).

196. **PTI-125/Simufilam Blocks the Interaction Between  $\beta$ -amyloid (“A $\beta$ ”) and  $\alpha$ 7-Nicotinic Acetylcholine Receptors (“ $\alpha$ 7nAChR”).** *Fourth*, most of the Western blots in these papers take advantage of a process known as co-immunoprecipitation. In this technique, tissue is ground up until it is liquefied and an antibody is used to catch a protein of interest. When the antibody and the protein it binds to are isolated, any other proteins that bind to the target protein will also be isolated. This approach enables scientists to evaluate if two proteins interact with each other.

197. As a standard laboratory practice, the first step in evaluating a co-immunoprecipitation sample is to perform a Western blot to confirm that the target protein was captured. It does not make sense to proceed to analyze other proteins if the target protein was not captured. Drs. Wang and Burns consistently follow this convention, including in the examples below.

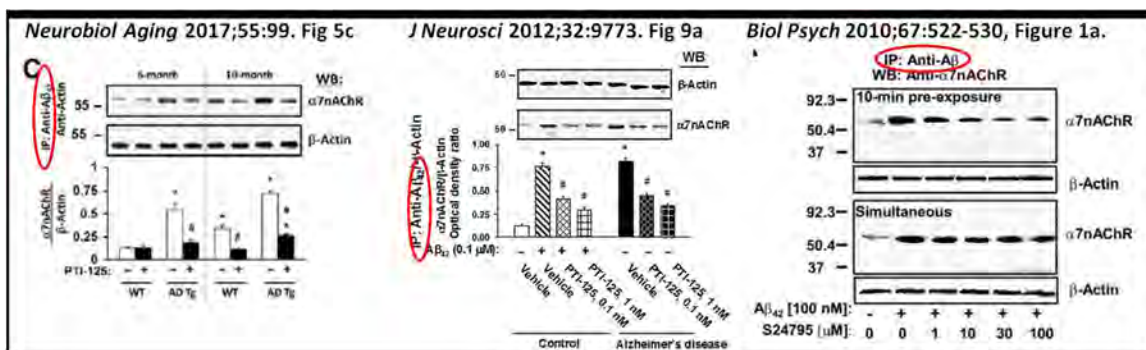


198. The Citizen Petition, however, noted that “there is one exception. The control blot demonstrating efficient capture of the target protein is omitted every time co-immunoprecipitation of  $\beta$ -amyloid is presented. A series of these co-immunoprecipitation experiments is shown below, each omitting this necessary blot. There are numerous other examples throughout the publications. The authors

used this technique to build the case that  $\beta$ -amyloid interacts with  $\alpha 7$ -nicotinic acetylcholine receptors.”

According to the petition authors:

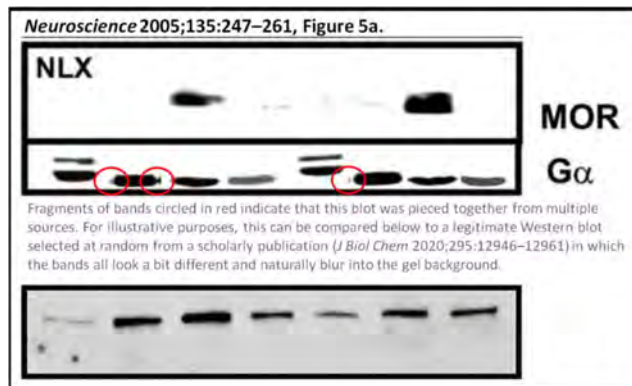
The fact that they *deviated from a standard of practice* they strictly follow in other settings is suspicious. It is also noteworthy that a significant fraction of the western blots shown elsewhere in the document to have been manipulated are associated with  $\beta$ -amyloid co-immunoprecipitation experiments (the center and right example in the figure following also contain two of the more-egregious examples of western blot falsification).



199. The Citizen Petition concluded that “[t]hese observations strongly call into question the assertion that PTI-125/simufilam alters the interaction between  $\beta$ -amyloid and any of its supposed targets.”

(2) **Western Blot Manipulation in an Additional Study by Drs. Wang and Burns - *Neuroscience* 2005 [Figures 5A, 5B, 12A, 2, 3]**

200. The Citizen Petition revealed that in **Figure 5A** of their 2005 *Neuroscience* paper, “Ultra-low-dose naloxone suppresses opioid tolerance, dependence and associated changes in mu opioid receptor-G protein coupling and Gbetagamma signaling,” Drs. Wang and Burns appear to have “spliced together” gels from different experiments. According to the petition, “[t]elltale signs that the Gα bands in **Figure 5A** likely come from different gels are circled in red below. The cropped borders of an adjacent protein band are present indicating the bands were taken from another blot.”

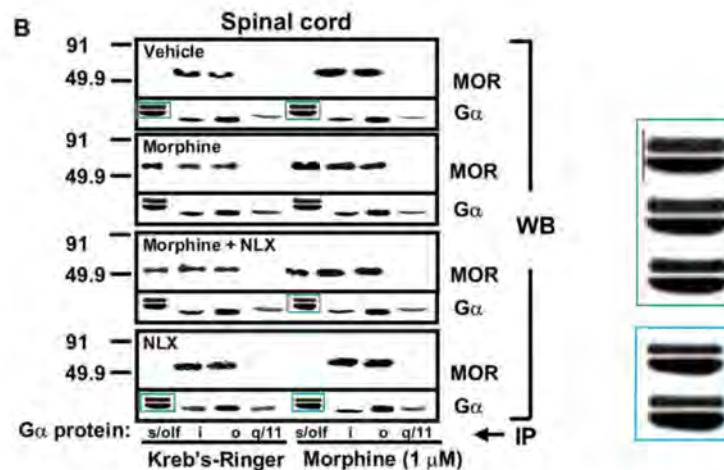


201. Dr. Rossner agreed with this analysis. Based on the presence of the sharp edges, he is highly confident *that the image panel in question has been spliced*. There appear to be remnants of previously neighboring bands that have been cut off on both sides of the left-hand band and on the left side of the right-hand band.

202. Moreover, if the Gα panel is spliced and the corresponding MOR experimental panel above it is not spliced, then the two proteins were detected on different blots. In that case, the MOR blot was not stripped and re-probed with antibodies against various Gα proteins, as claimed in the published figure legend, and the conclusion derived from this part of **Figure 5A** is unreliable because there is no valid immunoprecipitation control for the NLX treatment.

203. The Citizen Petition also stated that “[i]n the 2005 Wang and Burns paper *Neuroscience* 135 247-261, one can see bands with unique features that appear spliced into multiple gels. This suggests that experiments were not conducted as described.” One example of this is **Figure 5B** (below). In this Western blot, “the Gα bands in the s/olf lanes have peculiar ‘double decker’ shapes. Close inspection reveals that three of these double decker bands (green) are more similar to each other than would be expected AND another two of these double deckers (blue) are also more similar to each other than would be expected.” The petition concluded that the “congruence of these oddly shaped bands are *unlikely to have occurred by chance* and raises the possibility of band duplication and data manipulation.”



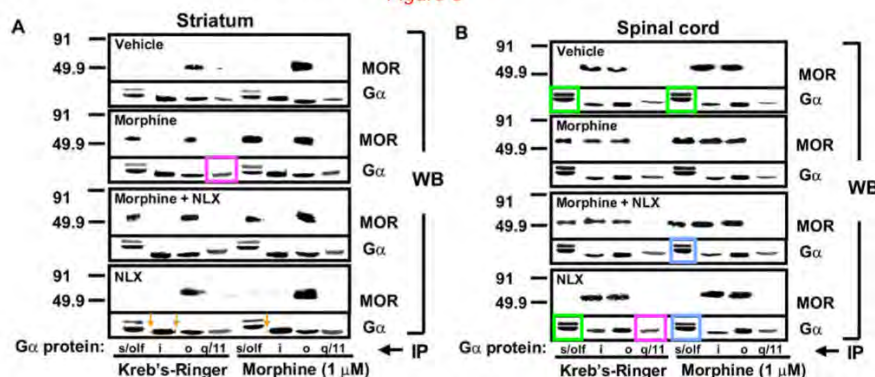


204. Dr. Rossner concurred with the Citizen Petition's assessment for the top right and bottom bands in green boxes and in the top bands in the blue box.

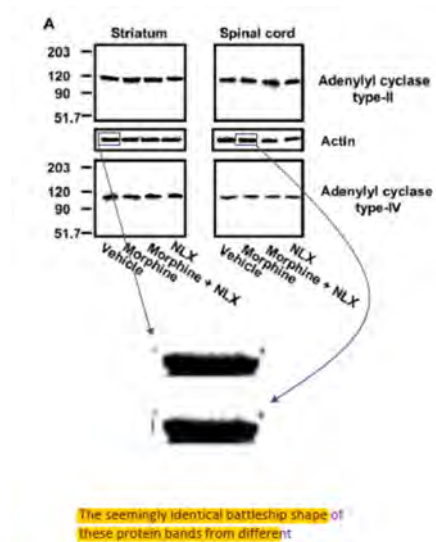
205. Regarding **Figures 5A and 5B**, Dr. Bik agreed, noting, "several bands that look similar." Specifically, she described on PubPeer:

- Blue and green boxes: It was noted in the report mentioned above that some of the "double decker" bands look similar to each other. The resolution is low, but maybe the authors could take away these concerns by showing the uncropped blots, if they still are available?
- Pink boxes: An additional concern not noted in the [Citizen Petition] is that two of the G-alpha bands, representing seemingly different experiments (Morphine vs NLX), look quite similar, while their surrounding bands are very different.
- Orange arrows: some artifacts around bands suggestive of splicing.

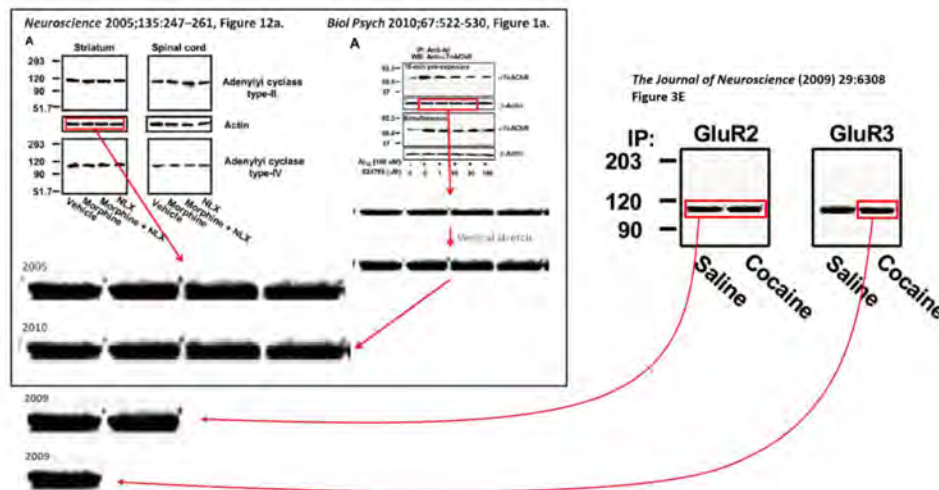
252

H.-Y. Wang et al. / Neuroscience 135 (2005) 247–261  
Figure 5

206. The Citizen Petition then identified another “striking example of probable band duplication” in **Figure 12A** of the paper (below). There, “the actin band from the striatum brain region treated with ‘Vehicle’ is indistinguishable from the actin band from the spinal cord region treated with Morphine. The uncanny resemblance of these ‘battleship’ shaped bands and the precise alignment of the dot artifacts suggest that one or both were *intentionally inserted*, perhaps with the intention of *misrepresenting the results*.”



207. In fact, as described in the Citizen Petition and the petition’s third supplement, dated November 17, 2021, this figure contains images that were apparently duplicated and “reused” to represent *three entirely different proteins*, in three *entirely different experiments*, in three *entirely different publications*, including the 2005 *Neuroscience*, 2009 *Journal of Neuroscience*, and 2010 *Biological Psychiatry* papers. See below. The Citizen Petition concluded: “***This degree of congruence [between Figures 12A and 1A] could not have occurred by chance or error***; it suggests a complex cross-publication dimension to Cassava Science’s band duplication behavior and, in this case, it is hard to imagine that the duplication was not intentional.”

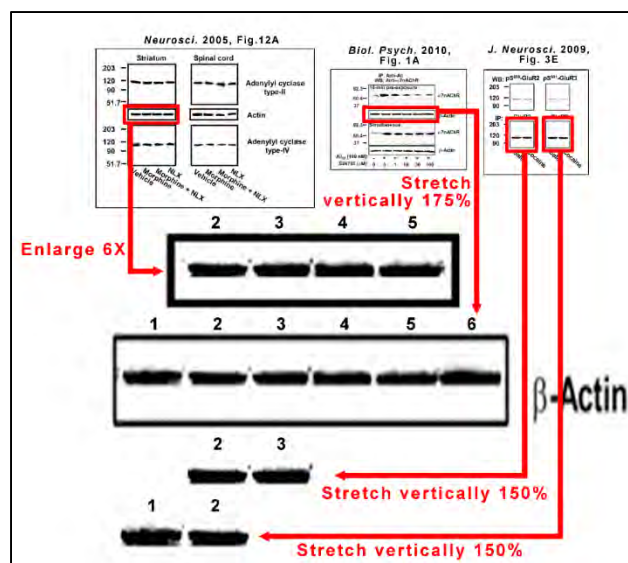


208. In her August 27, 2021 blog post, Dr. Bik concurred with this assessment, stating the blot “appears to have been reused in the *Biological Psychiatry* (2010) paper, where it represented a different experiment.”

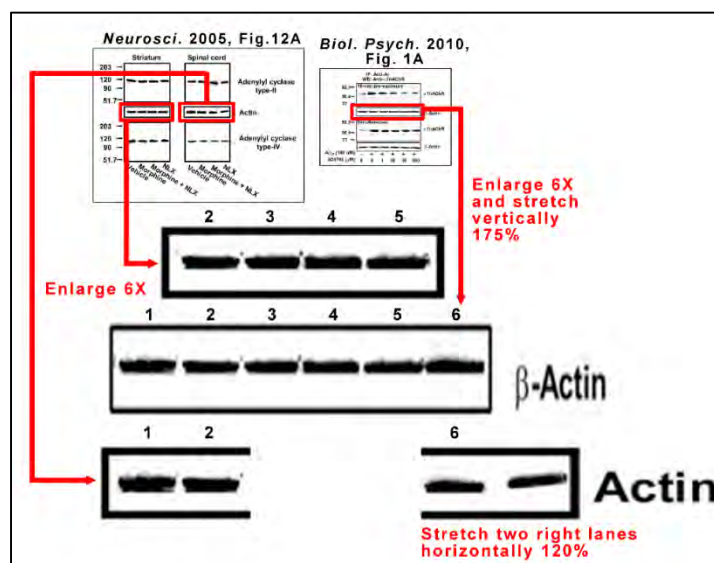
209. Dr. Bik further detailed her findings on PubPeer, describing “[a] similarity of a **Figure 12A** Actin blot [from the 2005 *Neuroscience* paper] with an Actin blot in **Figure 1A** of Wang et al., *Biological Psychiatry* (2010), DOI: 10.1016/j.biopsych.2009.09.031 [that] was discussed in [the Citizen Petition] letter to the FDA” and noting [this was] “not my own finding, but I agree with the similarity.”

210. Dr. Bik also agreed with the Citizen Petition that “the left most Actin lane in ‘Striatum’ section of **Figure 12A** of this [2005 *Neuroscience*] paper looks remarkably similar to the second-from-the-left Actin lane in the ‘Spinal Cord’ section.”

211. Similarly, Dr. Rossner concluded with high confidence that, as seen below, based on the similar band shapes, sizes, edge elements, background elements, internal intensity variations, and relative positions, the vertically aligned bands with the same lane number are duplicates derived from the same source image. *Thus they cannot depict different samples or different proteins as claimed in the figures.*

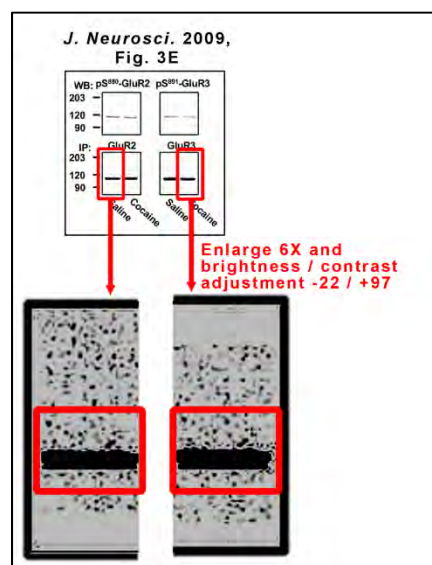


212. Dr. Rossner further concluded that there is also an apparent duplication between the two Actin panels in **Figure 12A** in the *Neuroscience* 2005 article, rendering that result unreliable, as reflected below.



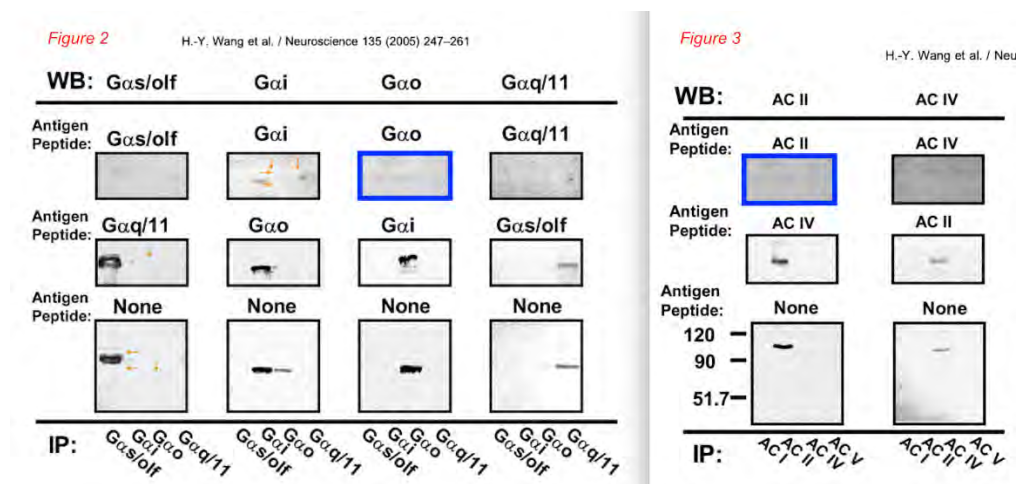
213. Based on similar band shapes, sizes, edge elements, background elements, internal intensity variations, and relative positions, Dr. Rossner concluded with high confidence that the vertically aligned bands *are duplicates derived from the same source image in the above two panels within the 2005 Neuroscience article. Thus they cannot depict different samples as claimed in the figures.*

214. And upon further examination, Dr. Rossner also found that there was an additional duplication within Dr. Wang's 2009 *Journal of Neuroscience* paper, "Prenatal Cocaine Reduces AMPA Receptor Synaptic Expression through Hyperphosphorylation of the Synaptic Anchoring Protein GRIP," mentioned in the Citizen Petition above. Dr. Rossner concluded with high confidence that *the highlighted regions below in Figure 3E are duplicates derived from the same source image*. The differences are likely due to image compression steps in the figure preparation and/or publication processes.



215. Dr. Bik further found, as she described on PubPeer, "[a]dditional concerns about **Figures 2 and 3** [in Drs. Wang's and Burns's 2005 *Neuroscience* paper], not mentioned in the [Citizen Petition]":

- Blue boxes: The top Gαo panel in **Figure 2** is very similar to the ACII panel in **Figure 3**. Based on the labels, these appear to be representing different samples or experiments.
- Orange arrows: Unexpected sharp background transitions around certain bands or between lanes. Of particular note is the top Gαi panel in **Figure 2**, where the third band appears to be surrounded by a rectangularly shaped area that does not match the rest of the blot.



A close-up of the  $G\alpha i$  panel in **Figure 2**, made darker to bring out the distinct background indicative of manipulation is below.

**$G\alpha i$**



216. This and the other evidence of intentional data manipulation detailed throughout demonstrates a pattern of scientific misconduct that undercuts the foundational science related to simufilam's mechanism of action for treating Alzheimer's disease.<sup>2</sup>

#### b. Integrity of the Phase 2b Clinical Biomarker Data

217. As described above, on May 15, 2020, Cassava reported that its Phase 2b trial missed its primary endpoints. But, on September 14, 2020, Cassava reversed course and reported that the first analysis was an error, and that when patient samples were again tested and finalized, simufilam robustly

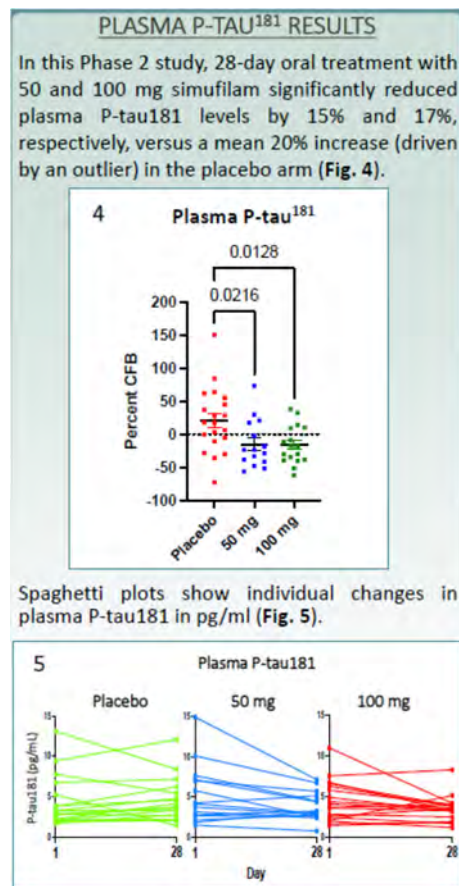
<sup>2</sup> The 2005 *Neuroscience* paper describes a molecular signaling pathway associated with ultra-low dose naloxone that Drs. Wang and Burns later allege involves a high affinity binding site on filamin A that also binds to simufilam. The 2010 *Biological Psychiatry* paper describes a cascade of A $\beta$ 42 binding to the  $\alpha 7$ nAChR that somehow leads to tau phosphorylation, which is the pathway that they have touted is interrupted by simufilam. Thus, both these papers also relate to Cassava's development of simufilam.



improved all biomarkers. The Citizen Petition, however, rejected these claims and identified evidence indicating that these so called “final” results had been manipulated.

**(1) Cassava Manipulates Phase 2b Biomarker Results  
at the Alzheimer’s Association International  
Conference**

218. On July 26, 2021, Cassava presented a poster at the AAIC entitled “SavaDx, a Novel Plasma Biomarker to Detect Alzheimer’s Disease, Confirms Mechanism of Action of Simufilam” regarding their “final” clinical biomarkers results from the Phase 2b trial. The poster lists the names of Drs. Wang and Burns and another Cassava employee, George Thornton, among others, including Lynne Brunelle of Quanterix. **Figures 4 and 5** of this poster (below) describe effects of 28-day treatment with simufilam on the biomarker plasma P-tau181. High P-tau181 plasma levels are correlated with the development of Alzheimer’s disease dementia, and are considered a diagnostic and prognostic biomarker of Alzheimer’s disease. The two figures purported to show the *same data* in two different ways: (i) **Figure 4** shows the percent change from baseline; and (ii) **Figure 5** shows the absolute biomarker values for individuals before and after treatment. There are, however, discrepancies between the data evidencing manipulation, as detailed in the Citizen Petition.



219. The Citizen Petition highlighted that these clinical biomarker data present “two significant problems.” First, that it was concealed from the public that Dr. Wang conducted the Phase 2b reanalysis. Second, that the plasma biomarker data in the poster contains evidence of manipulation. Specifically, a key data point is missing from **Figure 4** in the 100 mg group that is present in the 100 mg group for **Figure 5** in the presentation.

220. As the first supplement to the Citizen Petition, dated August 30, 2021, described in detail, Aaron Fletcher, Ph.D., of Bios Research, a financial services firm that provides public equity research in the healthcare space, performed an analyses on the poster’s figures, which was then provided to Drs. Bredt and Pitt. Dr. Fletcher confirmed that a point was missing from **Figure 4** in the 100 mg treatment group and further determined that the missing point should have reflected a ~+150% change from baseline.

221. This finding is significant because if the missing value for the 100 mg treatment group is inserted, the p-value changes from the Company’s reported value of ~0.01 to a *non-significant* p-value of



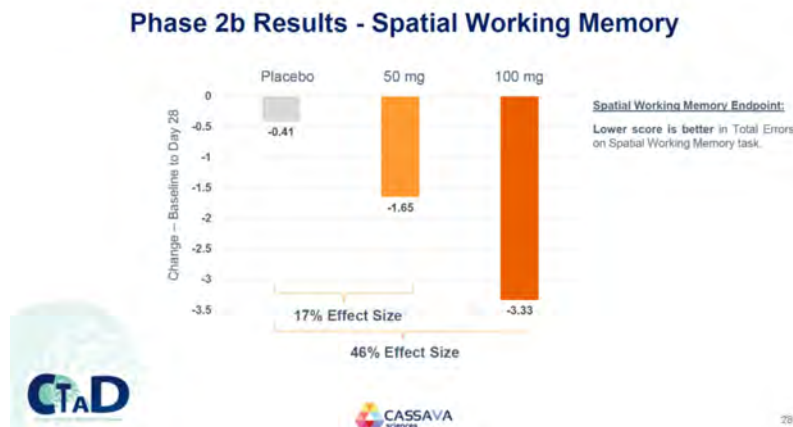
0.08. According to the Citizen Petition, when recalculating using paired t-tests accounting for that switch, the p-values for the 50 mg and 100 mg treatment groups become larger (0.034 and 0.15, respectively). Because the study evaluated multiple biomarkers, *neither of these groups would be considered statistically different from placebo* when accounting for multiple comparisons.

222. On August 30, 2021, Dr. Bik also posted a follow-up entry on her blog entitled “Cassava Sciences: Of Posters and Spaghetti Plots.” That post reviewed Cassava’s July 26, 2021 AAIC poster. Dr. Bik “*agree[d] with those concerns*” raised in the Citizen Petition regarding the data in **Figures 4 and 5**, and that the missing data point had been inserted into the placebo group rather than the 100 mg group where it belonged. She similarly noted that if the outlier data point from the poster had properly been included in the 100 mg treatment group, instead of the placebo group, “the average change-from-baseline would change from -17% to around -3%, which is a *much less spectacular reduction* of plasma P-tau181 levels than claimed by the company.”

**(2) Cassava Misstates Phase 2b Cognitive Results at the Conference on Clinical Trials on Alzheimer’s Disease**

223. The August 30, 2021 first supplement to the Citizen Petition identified additional errors, not previously included in the Citizen Petition, in Cassava’s data concerning their Phase 2b results as well. First, on November 7, 2020, Cassava presented its Phase 2b results at the Conference on Clinical Trials on Alzheimer’s Disease in a slide deck entitled “Sumifilam Significantly Improves Eleven CSF Biomarkers in a Randomized, Placebo-controlled, One-month Clinical Trial in Alzheimer’s Disease Patients.” This presentation was authored by Drs. Burns, Wang, and Friedmann, among others.

224. Slide 27 of the deck presents “key cognition results” from the Phase 2b trial Spatial Working Memory test, reproduced below:



225. The underlying data for these results were deposited by the Company on ClinicalTrials.gov but, as revealed by the Citizen Petition, they “do not support the data provided in the [November 2020] CTAD presentation.” The “change from Day 1 in total errors” data on ClinicalTrials.gov (below) does not match the data in the CTAD presentation (above). Specifically, the 50 mg result is -3.35 and the 100 mg result is -2.31 in the below data on ClinicalTrials.gov, which are not the same numbers included in the above slide.

8. Secondary Outcome

<b>Title</b>	Spatial Working Memory Test		
<b>Description</b>	Cognitive assessment of spatial working memory. A number of colored squares (boxes) are shown on the screen. By selecting the boxes and using a process of elimination, the subject should find one yellow 'token' in each of a number of boxes and use them to fill up an empty column on the right-hand side of the screen. The number of boxes is gradually increased to a total of 8 for the subjects to search. The colors and positions of the boxes are changed from trial to trial to discourage stereotyped search strategies.		
<b>Time Frame</b>	Day 1 to Day 28		
<b>Outcome Measure Data</b>	<p><b>Analysis Population Description</b></p> <p>Removed from analysis were the 3 patients with no detectable drug in plasma, 2 patients with <math>\geq 25\%</math> non-compliance by pill counts, one patient with no baseline test and one who did not understand instructions per rater notes.</p>		
<b>Arm/Group Title</b>	Placebo Cohort	Simufilam (PTI-125), 100 mg Tablets Cohort	Simufilam (PTI-125), 50 mg Tablets Cohort
<b>Arm/Group Description</b>	Placebo oral tablets administered twice daily (BID)	Simufilam, 100 mg oral tablets administered twice daily (BID)	Simufilam, 50 mg oral tablets administered twice daily (BID)
<b>Overall Number of Participants Analyzed</b>	22	18	17
<b>Mean (Standard Deviation)</b>			
<b>Unit of Measure: Change from Day 1 in total errors</b>	-0.41 (7.54)	-2.31 (7.45)	-3.35 (4.86)

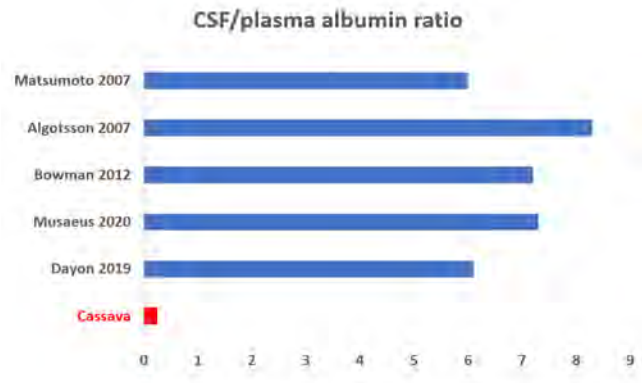
226. Further, in the ClinicalTrials.gov data (above) the 50 mg treatment group (*i.e.*, the smaller dose) demonstrated a greater difference than the 100 mg treatment group, and reflects that the purported

“effect” of simufilam in the dosage groups is compromised by inequivalent baseline measurements, as seven individuals were removed from the baseline Spatial Working Memory test in the 100 mg and 50 mg dose groups.

### (3) **Abnormalities in Cassava’s Phase 2b Biomarker Data**

227. On September 9, 2021, Drs. Bredt and Pitt filed a second supplement to the Citizen Petition, further confirming that Cassava’s Phase 2b data from the reanalysis suffered from abnormalities undermining its validity and reliability. Specifically, the September 9, 2021 second supplement revealed that “[m]any of the results from Dr. Wang’s Phase 2b redo have what appear to be data manipulation or GROSS LAB ERRORS – values *incompatible* with standards for these type of analyses – which raises additional questions about the validity of the biomarker results associated with the redo.”

228. The Phase 2b study looked at numerous “key” biomarker results. Three of these key biomarkers, however, suffered baseline measurement “far outside expectations” with “extreme variation from many other Alzheimer’s Disease (AD) biomarker studies,” suggesting “the redo has major lab errors or manipulation.” The first biomarker is the CSF/plasma albumin ratio, which is a clinical lab test and is fairly uniform across individuals (even with Alzheimer’s Disease) at 5-10. The September 9, 2021 second supplement noted that the following link from Allina Health (<https://account.allinahealth.org/library/content/49/150212>) advises elderly patients that they should expect a value of 8-9. But Dr. Wang measured *just 0.24* in the reanalysis. To highlight the discrepancy, exemplary published studies of CSF/plasma albumin in Alzheimer’s Disease compared to Cassava’s “redo” are provided below.



229. The second problematic assay concerned the baseline for IL-6, which is an inflammatory biomarker that is elevated in autoimmune diseases. As the second supplement noted, in other Alzheimer’s disease studies, CSF IL-6 levels are 1-5 pg / mg. Yet the baseline IL-6 averages Cassava reported in the reanalysis are **33-34pg / ml**. To highlight the discrepancy, exemplary published studies of CSF IL-6 levels in Alzheimer’s Disease patients compared to Cassava’s “redo” are provided below.



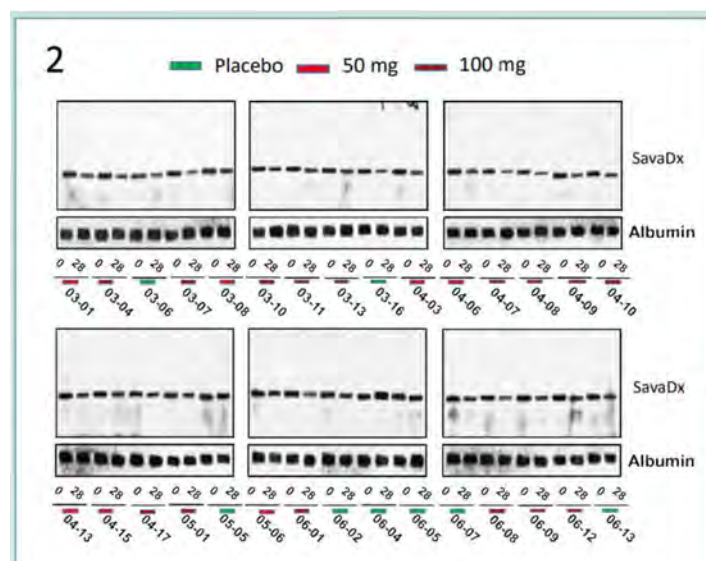
230. Third, the sTREM2 baseline in the “redo” was far outside other published studies. To highlight the discrepancy, exemplary published studies of CSF sTREM2 in Alzheimer’s disease compared to Cassava’s “redo” are provided below.



231. On September 11, 2021, William Hu, M.D., Ph.D., a prominent neurologist at University of Rutgers posted on Twitter that he *agreed* with these concerns.

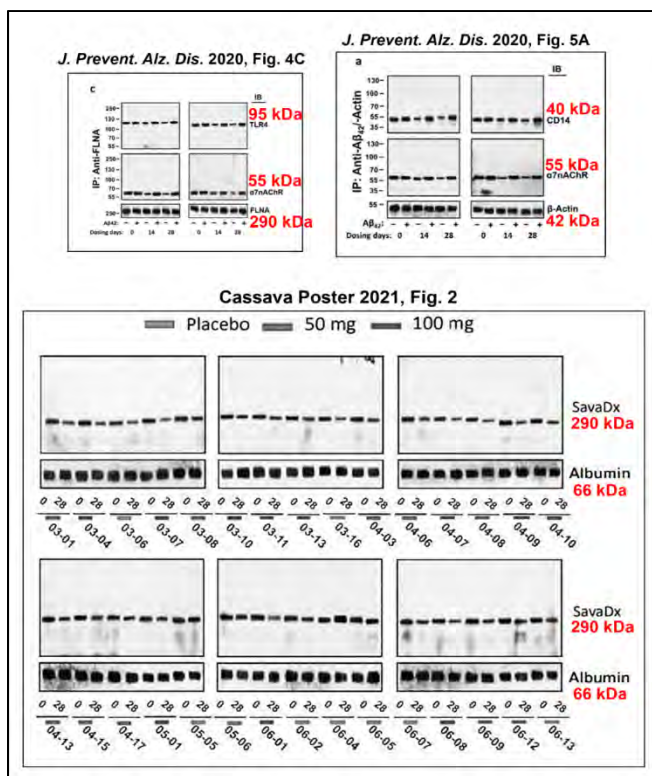
(4) **Cassava Misrepresents SavaDx Phase 2b Data at the Alzheimer's Association International Conference**

232. **Figure 2** (below) in Cassava's July 26, 2021 AAIC poster presentation is a collection of Western blots showing that treatment of Alzheimer's disease patients with simufilam lowers their plasma levels of "SavaDx," which the poster defines as "i.e. altered Filamin A levels." According to the Citizen Petition, "[o]wing to how large (290 kD) proteins run on gels, an experienced biochemist would advise that the blots in figure 2 likely *do not represent the 290 kD protein Filamin A*" represented in **Figure 2**.



233. Dr. Rossner concurred with the Citizen Petition's assessment. Such a large protein, like filamin A, would normally be present at the top of the blot (due to its high molecular weight), but the protein SavaDX bands in the poster (defined as altered filamin A) are present in the center of the blot.

234. In addition, the shapes and sizes of the bands are suspect. The bands labeled FLNA in **Figure 4C** in Cassava's 2020 *Journal of Prevention of Alzheimer's Disease* article, or  $\beta$ -Actin in **Figure 5A** in the same article, or Albumin in **Figure 2** in the Cassava 2021 AAIC poster presentation, all have similar shapes and sizes. This is unusual for proteins with such wide variations in molecular weight, as reflected below (protein molecular weights have been added in red for reference). Similarly, bands labelled TLR4,  $\alpha$ 7nAChR, CD14, or SavaDX (FLNA) in the three figures all have similar shapes and sizes *despite widely differing molecular weights*.



235. Dr. Rossner concluded that the concerns raised here render this data questionable.

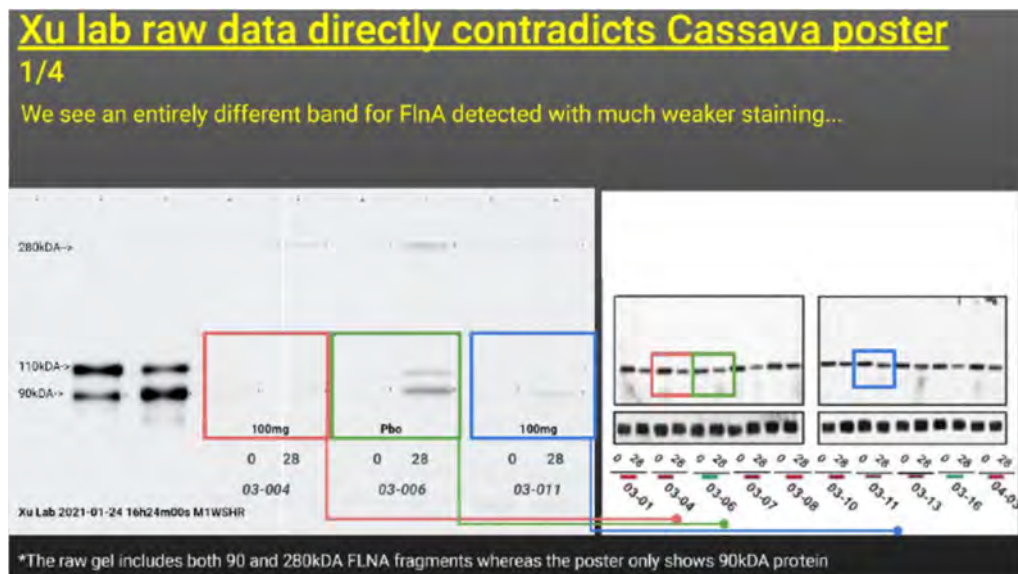
236. Furthermore, apparent direct evidence of data manipulation related to Cassava's 2021 AAIC poster presentation was documented by a group of scientists independently investigating Cassava,

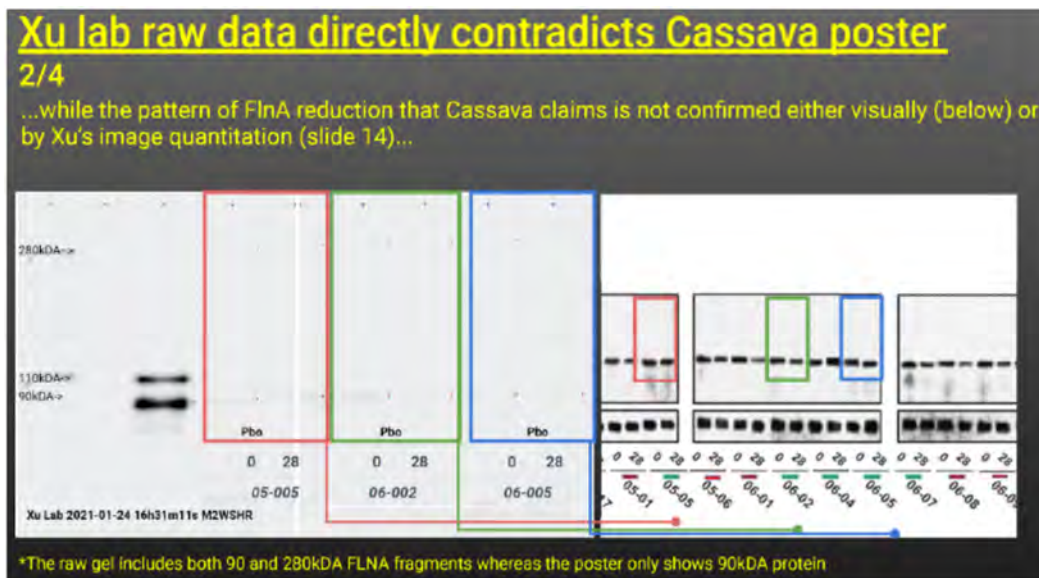


who also took short positions on the Company. They posted their concerns on Twitter and made a presentation of their findings, dated November 29, 2021, entitled “SAVADx: Theranos 2.0” available online at cassavafraud.com.

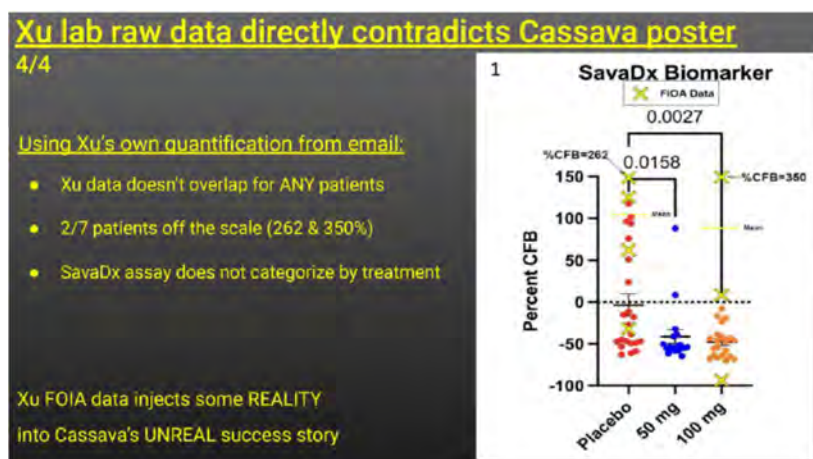
237. Through a FOIL request to CUNY, the scientists obtained a set of Dr. Wang’s emails containing raw data that appear to represent a subset of the experiments presented in Cassava’s July 26 AAIC poster. Cassava Senior Vice President of Technology and a member of the Company’s management team, Ben Thornton, was included on this email. Several apparent red flags arise when comparing the raw data in a January 24, 2021 email with the figures in Cassava’s AAIC poster.

238. **First**, Western blot images in an email from Dr. Xu of Abilene Christian University, a co-author of the poster, to Dr. Wang *look entirely different* from those presented in **Figure 2** of Cassava’s AAIC poster. The Western blots in Dr. Xu’s email are on the left in both panels and the data from **Figure 2** is presented on the right (below). The color-coded boxes indicate corresponding patient samples (note the corresponding sample IDs, *e.g.*, 03-04) in Dr. Xu’s data and the presentation of those data in **Figure 2** of the AAIC poster.





239. **Second**, the SavaDx values that the scientists calculated from Dr. Xu's data in the FOIL email look entirely different from those presented in **Figure 1** of Cassava's AAIC poster, as shown below.



240. Drs. Bredt and Pitt reviewed this information and concluded in a December 8, 2021 supplement to the Citizen Petition that “[w]hile we do not have access to the original emails obtained by the FOIA request, and we cannot be certain of the independent scientists’ calculation of SavaDx, their findings are consistent with the concerns my clients previously raised about the 26th July poster.”

### c. Integrity of the Phase 2a Clinical Biomarker Data

241. The Citizen Petition questioned the cerebrospinal fluid (or “CSF”) analysis performed on 13 patients in Cassava’s Phase 2a study. Drs. Wang, Burns, Barbier, and Friedmann, among others,

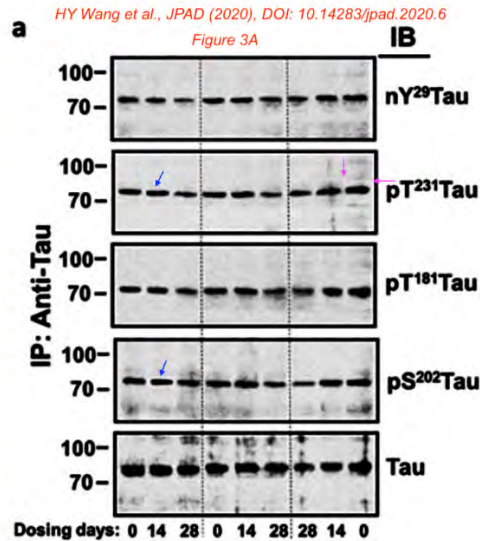


published the results of this study, “PTI-125 Reduces Biomarkers of Alzheimer’s Disease in Patients,” in 2020 in *The Journal of Prevention of Alzheimer’s Disease* (or “JPAD”). And, notably, the JPAD paper explicitly states that Cassava “monitored the conduct of the study and data collection.” The petition highlighted that, “[r]emarkably, this manuscript was accepted for publication Nov. 6, 2020 seven days after submission October 31, 2020. If those dates are correct, it seems highly unlikely to have been subjected to rigorous peer review.”

242. Data from this manuscript in **Figure 3A** was included in Cassava’s presentation at the 12th International Conference on Clinical Trials on Alzheimer’s Disease (“CTAD”) on December 5, 2019. In the August 30, 2021 first supplement to the Citizen Petition, Drs. Bredt and Pitt noted that Dr. Bik, “confirmed our analysis of this image,” “expressed major concerns with the integrity of these phase 2a data and advised the inspection of the original images is needed to assess the authenticity of the clinical study results.”

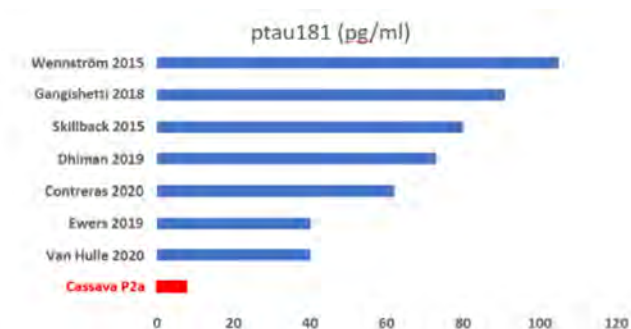
243. Indeed, Dr. Bik had written in her August 27, 2021 blog post that “[t]he third and most recent paper, JPAD 2020, was mentioned in the [Citizen Petition] report because it was submitted to the journal on October 31, 2019, and accepted on November 6, 2019. Usually peer review take anything from one to many months, so a peer review turned around in a week is *remarkably fast*.”

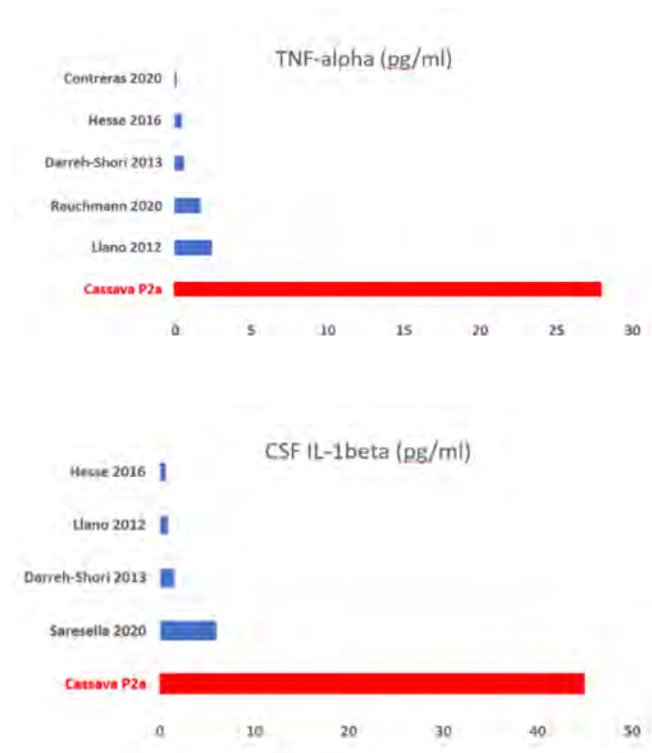
244. More importantly, however, she raised an additional manipulation concern, noting that although “[t]he [Citizen Petition] report did not mention any image problems,” **Figure 3A** of the paper “appears to show a rectangular box around one of the pT231Tau bands. It is shown below with pink arrows.” In addition, “[s]ome other bands, shown with blue arrows, appear to be surrounded by a white halo and to float above the background. The latter concern could just be a compression artifact, although it is not seen in all bands, just in a couple.”



245. Then, in their November 17, 2021 third supplement to the Citizen Petition, Drs. Bredt and Pitt found that “at least three of the nine biomarkers analyzed by Dr. Wang and published by Cassava for the Phase 2a study of simufilam in Alzheimer’s disease also appear to have *wildly anomalous baseline measures*,” similar to the abnormal biomarkers results presented by Cassava in the Phase 2b study of simufilam in Alzheimer’s disease, with “baseline values so far outside expectations that they suggest *lab errors or manipulation*.”

246. Specifically, “CSF levels of pTau-181 are far lower, whereas CSF levels of TNF- $\alpha$  and IL-1 $\beta$  are far higher, than in other biomarker studies of Alzheimer’s disease patients.” See below.





247. Cassava’s anomalous Phase 2a biomarker data undermines the integrity and validity of the Phase 2a data, especially given Cassava’s later rejection of so-called “anomalous” data that the Company received in the initial analysis of its Phase 2b results, which the Company declared invalid. Moreover, Defendants’ rejection of negative Phase 2b results on the grounds that the data was “anomalous,” while accepting other anomalous but purportedly positive Phase 2a and 2b data, further undermines the validity and integrity of Cassava’s Phase 2 trial results.

#### **d. Integrity of the Analysis Involving Human Brain Tissue**

248. Cassava claims simufilam binds to filamin A and alters its conformation. In so doing, it allegedly blocks the interaction between  $\beta$ -amyloid and the  $\alpha 7$ -nicotinic acetylcholine receptor. This supposedly modifies a range of downstream molecules and signaling pathways including NMDA signaling, Toll-like receptor signaling (causing an anti-inflammatory effect) and decreasing tau phosphorylation.

249. This is a complex mechanism. In one key line of experiments, Drs. Wang and Burns report that this entire mechanism can be observed in post-mortem human brain tissue from subjects with Alzheimer's disease and neurological controls. This data is contained in their 2017 *Neurobiology of Aging* paper, which builds on similar experiments in Dr. Wang's 2009 *The Journal of Neuroscience* paper and their 2012 *The Journal of Neuroscience* paper.

250. In these experiments, post-mortem human brain tissue is warmed from -80°C to -20°C and chopped into blocks. The resulting chopped tissue is treated with  $\beta$ -amyloid and the experimental drug for one hour. They then report a massive increase in tau phosphorylation (modification of the tau protein by enzymatic addition of a phosphate group to the protein; up to 10 fold) from  $\beta$ -amyloid treatment in untreated samples; and that tau phosphorylation was blocked by addition of simufilam. According to the Citizen Petition, "[i]t is unlikely that the enzyme responsible for phosphorylation would survive the initial -80°C freezing step. Moreover, the phosphorylation experiments are reported to have been performed at 4°C, but it is unlikely that the enzyme responsible for phosphorylation would be active at 4°C (enzymes generally work best at body temperature – 37°C)." Moreover the "results are premised on the enzymes in the human brain extracts remaining active up to 13 hours post-mortem before freezing, remaining active after nearly 10 years in frozen archival without any advanced cryopreservative techniques, and being active at 4°C."

251. The Citizen Petition concluded:

The complex, multi-step cellular processes the authors claim to observe in tissue that has been dead for a decade are contrary to a basic understanding of neurobiology. Claims of this magnitude require extensive, detailed verification, but the authors provide no evidence of tissue viability. We are not aware of any other research group which has effectively used this technique. As with the western blot data, ***there are anomalies in the presentation of the data from this human tissue, which again strongly suggest manipulation.***

**H. Following Cassava’s Rebranding, Defendants Repeatedly Highlight the Company’s Pre-clinical and Clinical Results for Investors Leading Up to the Class Period**

252. Since the time the Company re-branded as Cassava in 2019, Defendants have repeatedly made statements to investors promoting the pre-clinical and clinical research supporting simufilam.

**1. Cassava Touts the Pre-Clinical Research Forming the Basis of Simufilam’s Development as a Alzheimer’s Treatment**

253. On March 27, 2019, Cassava filed a Form 8-K with the SEC attaching a press release entitled “Pain Therapeutics Announces Name Change to Cassava Sciences, Inc.” In the press release, which was reviewed and approved by Barbier and Schoen, the Company stated: “*The underlying science for our programs in neurodegeneration is published in several prestigious, peer-reviewed technical journals, including Journal of Neuroscience, Neurobiology of Aging, and Journal of Biological Chemistry.*” Cassava, indeed repeatedly touted its published pre-clinical research as a basis for simufilam’s continued development as a treatment for Alzheimer’s disease both before and during the Class Period, highlighting its importance.<sup>3</sup>

254. On March 29, 2019, Cassava filed its 2018 Form 10-K with the SEC. The Form 10-K was signed by Barbier, Schoen, and Friedmann and made numerous claims trumpeting Cassava’s published pre-clinical research. The 2018 Form 10-K stated: “*PTI-125 benefits from a strong scientific rationale, peer-reviewed publications in prestigious academic journals and multiple peer-reviewed research grant awards from the [NIH], the primary agency of the U.S. government for biomedical research.*”<sup>4</sup>

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<sup>3</sup> This statement, with minor variations, was repeated in Cassava SEC filings, specifically: (i) Cassava’s Form 8-K filed with the SEC on April 29, 2019; (ii) Cassava’s Form 8-K filed with the SEC on August 12, 2019; (iii) Cassava’s Form 8-K filed with the SEC on September 9, 2019; (iv) Cassava’s Form 8-K filed with the SEC on October 29, 2019; and (v) Cassava’s Form 8-K filed with the SEC on December 6, 2019. Each Form 8-K and press release was reviewed and approved by Barbier and Schoen.

<sup>4</sup> This statement was repeated in Cassava SEC filings, specifically: Cassava’s Form 10-Q for the first quarter of 2019, filed with the SEC on May 2, 2019; Cassava’s Form 10-Q for the second quarter of 2019, filed with the SEC on August 12, 2019; and Cassava’s Form 10-Q for the third

255. The 2018 Form 10-K further stated:

*We believe there is experimental evidence for improving brain health by restoring altered FLNA with PTI-125, our lead product candidate. PTI-125 is a proprietary small molecule drug that represents an entirely new scientific approach to treat neurodegeneration. Published studies have demonstrated that PTI-125 targets an altered form of a protein called FLNA that is widely found in the Alzheimer’s brain.*

256. The 2018 Form 10-K continued, “[g]iven the absence of dose-limiting effects in healthy adults in a Phase I study, *a strong scientific rationale, and multiple peer-reviewed publications and research grant awards, we believe this program demonstrated favorable proof-of principle for the development of PTI-125 in Alzheimer’s disease.*”

257. The 2018 Form 10-K then stated:

*Over the past ten years, we successfully conducted basic research, and in vitro and preclinical studies in support of an [IND] submission to the FDA for PTI-125, including requisite studies around safety pharmacology, genetic toxicology and bioanalytical methods. In 2017 we filed an IND submission to the FDA for PTI-125.*

## 2. Statements Reporting the Results of Cassava’s Phase 2a Clinical Trial and Ongoing Development Program

258. Prior to the Citizen Petition, Cassava also repeatedly promoted its “promising” Phase 2a results, highlighting their importance, and continued to emphasize its published pre-clinical research. On September 9, 2019, Cassava filed a Form 8-K attaching a press release entitled “Cassava Sciences Reports Positive Phase 2a Clinical Results in Alzheimer’s Patients,” which was reviewed and approved by Barbier, Schoen, and Friedmann. The press release stated, in relevant part:

Lead drug candidate, PTI-125, *significantly decreased key biomarkers of neuroinflammation and neurodegeneration in all study patients (p<.001)*

*Clinical data support initiation of a Phase 2b study in Alzheimer’s in Q3 2019*

\* \* \*

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quarter of 2019, filed on with the SEC on October 29, 2019. Each of these filings was signed by Barbier and Schoen.

***“We conclude from this study that PTI-125 was able to reduce biomarkers of neurodegeneration and neuroinflammation in Alzheimer’s patients at a dose that appears safe and well-tolerated,”*** said Nadav Friedmann, PhD, MD, Chief Medical Officer of Cassava Sciences. ***“To our knowledge, no other drug has shown such promising results on objective, validated biomarkers of disease.”***

\* \* \*

***“We are excited to lead the way in the effort to bring a new treatment paradigm to Alzheimer’s, a disease that has seen few scientific advancements to date despite massive research efforts,”*** said Remi Barbier, President & CEO of Cassava Sciences. “The relationship between biomarkers and Alzheimer’s disease is crucial, well-known and widely published. As a result, we’re cautiously optimistic that PTI-125 moves us closer towards the goal of a disease-modifying treatment. And as always, we are grateful for the support of our collaborators, advisors and NIH, whose peer-review system of evaluation has enabled us to advance PTI-125 step-wise from basic research to clinical testing within 10 years.”

259. On December 6, 2019, Cassava filed a Form 8-K with the SEC attaching a press release, dated December 5, 2019, entitled “Cassava Sciences Announced Additional Positive Phase 2a Clinical Data in Alzheimer’s Disease at CTAD 2019,” and a December 5, 2019 presentation by Dr. Burns, which included Drs. Friedmann and Wang as contributors, at the CTAD entitled “One-month Oral Treatment with PTI-125, a New Drug Candidate, Reduced CSF & Plasma Biomarkers of Alzheimer’s Disease.”

260. The presentation specifically disclosed that Dr. Wang is a Cassava consultant and that his lab conducted the biomarker analysis for the Phase 2a trial, stating that Dr. Wang was a “consultant[] to Cassava Sciences” and that he “performed biomarker assays,” with two others who were “affiliated with” CUNY.

261. The presentation stated that the “[c]linical results from a first-in-patient study support PTI-125’s mechanism of action” and that the ***“clinical biomarker results are consistent with > 10 years of basic science and preclinical data.”***

262. In the “Conclusions” section, the presentation stated:

Phase 2a data are . . . .

Promising because:



- ***PTI-125 improved all biomarkers of AD pathology, neurodegeneration and neuroinflammation.***

263. As a result, the presentation concluded that the Phase 2a study demonstrated “[c]linical validation for FLNA as a target for AD drug development.”

264. The accompanying December 5, 2019 press release, which was approved by Barbier and Schoen and attached to the Form 8-K, repeated similar claims from the presentation. Specifically, the press release stated:

***Consistent with over 10 years of basic research and pre-clinical data, the new data show clinical evidence of PTI-125’s mechanism of action and drug-target engagement.***

265. On March 26, 2020, Cassava filed its 2019 Form 10-K, which was signed by Barbier, Schoen, and Friedmann. The 2019 Form 10-K stated, in relevant part:

In 2019, a small, first-in-patient, clinical proof-of-concept Phase 2a study funded by NIH, showed that open-label treatment with PTI-125 for 28 days ***significantly improved key biomarkers of Alzheimer’s pathology, neuroinflammation and neurodegeneration*** (p<0.001).

\* \* \*

*IND submission to FDA.*

***Over the past ten years, we successfully conducted basic research, in vitro studies and preclinical studies in support of an [IND] submission to the FDA for PTI-125, including requisite studies around safety pharmacology, toxicology, genotoxicity and bioanalytical methods. In 2017 we filed an IND with FDA for PTI-125.***

\* \* \*

Given the absence of any observable dose-limiting effects in healthy adults in a Phase 1 study, ***a strong scientific rationale, and multiple peer-reviewed publications and research grant awards, we believe this program demonstrated favorable proof-of-principle for the development of PTI-125 in Alzheimer’s disease.***

\* \* \*

***Consistent with over 10 years of basic research and pre-clinical data, we believe our Phase 2a study showed clinical evidence of PTI-125’s mechanism of action and drug-target engagement.***

\* \* \*



In February 2020, our Phase 2a study was published in *The Journal of Prevention of Alzheimer's Disease* (JPAD), a technical journal for the research community. ***This peer-reviewed publication highlighted that biomarkers of Alzheimer's disease pathology (P-tau, total tau and A $\beta$ 42), neurodegeneration (NfL and neurogranin) and neuroinflammation (YKL-40, IL-6, IL-1 $\beta$  and TNF $\alpha$ ) improved significantly after 28 days of treatment with PTI-125.***

266. On May 6, 2020, Cassava filed a Form 8-K with the SEC, attaching a press release, which was reviewed and approved by Barbier and Schoen, stating:

Cassava Sciences' lead therapeutic product candidate is for the treatment of Alzheimer's disease. PTI-125 is a proprietary, small molecule (oral) drug that restores the normal shape and function of altered filamin A (FLNA), a scaffolding protein, in the brain. Altered FLNA in the brain disrupts the normal function of neurons, leading to Alzheimer's pathology, neurodegeneration and neuroinflammation. ***The underlying science is published in peer-reviewed scientific journals, including Journal of Neuroscience, Neurobiology of Aging, Journal of Biological Chemistry and Journal of Prevention of Alzheimer's Disease.*** The Company is also developing an investigational diagnostic, called SavaDx, to detect Alzheimer's disease with a simple blood test.<sup>5</sup>

267. Just prior to the start of the Class Period, however, Cassava's purportedly "consistent" pre-clinical and clinical results fell apart in May 2020, when the Company announced that Cassava's Phase 2b trial failed to reach its primary endpoints. Undeterred, the Company stated it would conduct a controversial reanalysis of its Phase 2b data. The Class Period begins with Cassava's announcement regarding the results of that reanalysis.

## VI. FALSE AND MISLEADING STATEMENTS

### A. Statements Reporting the Results of Cassava's Phase 2b "Re-do" and Ongoing Development Program

268. The Class Period begins on September 14, 2020. On that date, Cassava filed a Form 8-K with the SEC, which was reviewed and approved by Barbier, Friedmann, and Schoen. The 8-K attached a press release entitled "Cassava Sciences Announces Final Results of a Phase 2b Clinical Study of

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<sup>5</sup> This statement was repeated in Cassava press releases dated June 3, 2020, September 14, 2020, November 4, 2020, February 2, 2021, February 8, 2021, and March 23, 2021. Each of the press releases was reviewed and approved by Barbier and Schoen. To the extent the statement was repeated during the Class Period, it is alleged as a false and misleading statement herein.

Sumifilam [sic] in Patients with Alzheimer’s Disease,” and a presentation entitled “Cassava Sciences, Inc. Final Results of a Phase 2b Study of Sumifilam [sic] in Alzheimer’s Disease,” dated September 14, 2020, which announced that the Company would host a conference call that morning led by Barbier, Friedmann, Burns and Schoen.

269. The press release announced “key” biomarker and cognition study results, and stated, in relevant part:

Cassava Sciences, Inc. today announced final results of a Phase 2b study with its lead drug candidate, sumifilam [sic], in Alzheimer’s disease. *In a clinical study funded by the [NIH], sumifilam [sic] significantly improved an entire panel of validated biomarkers of disease in patients with Alzheimer’s disease.* The ability to improve multiple biomarkers from distinct biological pathways with one drug has never been shown before in patients with Alzheimer’s disease. Study results are expected to be published in a peer-reviewed publication.<sup>6</sup> Sumifilam [sic] is the first of a new class of drug compounds that bind to a protein called Filamin A.

270. The press release quoted Barbier as stating:

“Other than a few drugs to help ease the decline, there’s really nothing out there to treat people with Alzheimer’s . . . . *The improvement on multiple biomarkers in this clinical study is a first and offers hope that sumifilam [sic] has potential to become a transformative treatment for people with Alzheimer’s disease.*”

271. Moreover, the press release stated that “[a]ll CSF samples *were sent to outside labs for bioanalysis*” to measure the biomarkers and that “[a]n academic lab generated final results.” The press release continued:

As previously disclosed, an initial bioanalysis by a different lab showed *highly anomalous data*, e.g., huge swings (in both directions) in levels of biomarkers, as well as biomarkers moving in opposite directions in the same patients, all in the group who took placebo for 28 days. *With its validity in question, the initial bioanalysis serves no useful purpose.*

272. The press release concluded:

### Phase 2b Study Conclusions

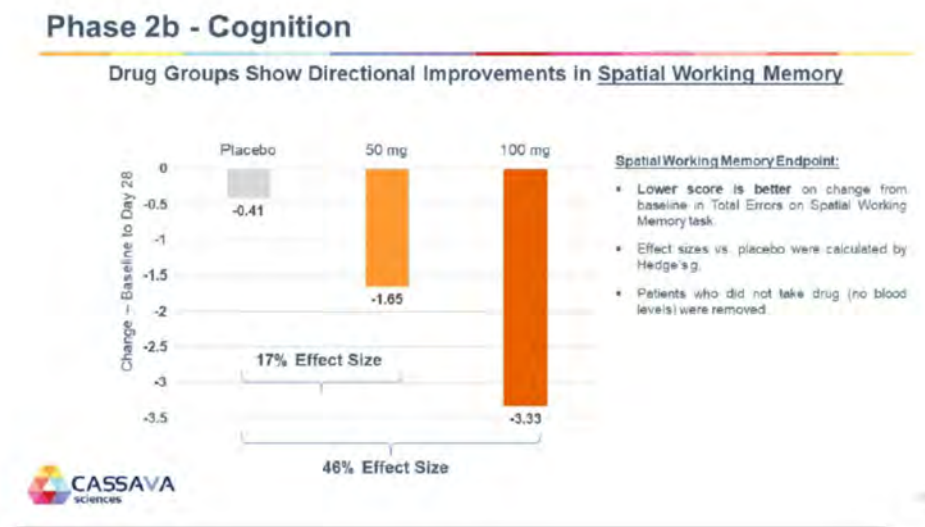
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<sup>6</sup> The results of Cassava’s “final” Phase 2b analysis have yet to be published in a peer reviewed journal.

A small, well-controlled study of sumifilam [sic] showed promising treatment effects in patients with mild-to-moderate Alzheimer's disease. In this study, sumifilam [sic] treatment over 28 days *improved an entire panel of validated biomarkers of Alzheimer's disease, decreased measurements of neuroinflammation, showed a 98% responder rate, appears safe and well-tolerated, and appears to benefit cognition. Importantly, the data are consistent with prior clinical and preclinical results, the drug's mechanism of action and over 10 years of basic research.*

273. The accompanying presentation reiterated that “[b]iomarker data received from that [first] lab made no sense. A post-hoc analysis showed significant data anomalies in patients who took placebo for 28 days” and that an “academic lab conducted a second, final bioanalysis of the Phase 2b study.”

274. The presentation further included a slide that stated: “Drug Groups Show Directional Improvements in Spatial Working Memory” and showed a *-1.65 result in the 50 mg group and -3.33 in the 100 mg group.*



275. During the conference call Barbier repeated that “sumifilam [sic] *significantly improved an entire panel of validated biomarkers* of disease in patients with Alzheimer's.”

276. Barbier further repeated that:

*An academic lab conducted a second and final biomarker analysis of the phase 2 data. The academic lab showed what we consider to be valid, proper and expected data in placebo patients.* The data from this lab shows modest swings, [inaudible] swings of course, maybe 4-6% on average, in level, in changes in levels of biomarkers over 28 days, but more importantly they showed biomarkers that generally moved in the same direction

and robust statistical correlations among changes in levels of biomarkers. ***For these reasons both ourselves and our advisors and pretty much anyone we’ve show all the data to have confirmed that the second bioanalysis is a valid analysis.***

277. During the presentation Dr. Burns also acclaimed Cassava’s pre-clinical and clinical research, stating:

***All this science, now on slide 14, has been published in peer reviewed journals starting in 2012 showing the filamin A was critical to this toxic signaling, 2017 showing that filamin A was in an altered conformation, and this year with the publication of our phase 2a clinical results. Sumifilam [sic] has also stood up to many peer reviewed NIH grant applications and received multiple NIH grant awards. So with all this science holding, holding it up, we, moving to slide 15, we were able to come up with the clinical hypothesis, can sumifilam [sic] provide early clinical evidence of disease modifying effect in a well-controlled study.***

278. Dr. Burns then presented the slides explaining that, in the so-called “final” Phase 2b results, the cognition test included a spatial memory test: “Slide 29 . . . show[ed] the effect on working spatial memory, the other test that we gave them. There was an impressive 46% effect size with the 100 mg dose group and a 17% effect size with the lower 50 mg dose group.”

279. Following the press release and investor conference call, Cassava’s stock price increased 133.4%, or \$4.43 per share, from \$3.32 per share to \$7.75 per share on September 14, 2020.

280. The next day, Barbier presented at the September 15, 2020 H.C. Wainwright 22nd Annual Global Investment Conference. There, he stated that PTI-125 “targets both neurodegenerative and neuroinflammation in Alzheimer’s Disease and it does this by binding to a single target. ***You don’t have to take our word for it. The underlying science is published in a number of peer reviewed journals and benefits from multiple recent clinical and non-clinical research grants from the NIH.***”

281. During his presentation, Barbier again announced that the underlying science had purportedly been vetted by experts: “***Again you don’t need to take our word for it. The underlying science for simufilan has been subject to the scrutiny of many experts in the field including the [NIH],*** which have awarded us over \$10 million in research grants.”

282. Barbier further exclaimed that “a *well-controlled Phase 2b study in simufilam showed promising treatment effects* in a population of mild to moderate AD patients” and that “[o]verall we feel that the dataset around simufilam really highlights this drug’s potential as a disease modifying drug candidate for Alzheimer’s Disease”

283. On November 4, 2020, Cassava filed a Form 8-K with the SEC, which was reviewed and approved by Barbier and Schoen, attaching a presentation entitled, “Sumifilam [sic] Significantly Improves Eleven CSF Biomarkers in a Randomized, Placebo-controlled, One-month Clinical Trial in Alzheimer’s Disease Patients” (“CTAD Presentation”), dated November 7, 2020, and a related press release entitled “Cassava Sciences Announces Additional Clinical Data from a Phase 2b Study of Sumifilam [sic] in Alzheimer’s Disease.”

284. The CTAD presentation, which provided results from Cassava’s Phase 2b trial and was authored by Drs. Burns, Wang, and Friedmann, among others, stated, in relevant part, that “[p]ublished preclinical and mechanism of action data support sumifilam’s [sic] potential as a disease-modifying drug for AD that may also enhance cognition” and that the “Study Conclusions” included that “Phase 2b treatment effects replicate prior clinical results and are consistent with published preclinical data and the drug’s mechanism of action.”

285. On November 9, 2020, Cassava filed its quarterly report with the SEC for the third quarter of 2020 on Form 10-Q. The Q3 2020 Form 10-Q was signed by Barbier and Schoen.

286. The Q3 2020 Form 10-Q stated, in relevant part:

Our lead therapeutic product candidate, sumifilam [sic], is a proprietary small molecule (oral) drug. Sumifilam [sic] targets an altered form of a protein called filamin A (“FLNA”) in the Alzheimer’s brain. *Published studies have demonstrated that the altered form of FLNA causes neuronal dysfunction, neuronal degeneration and neuroinflammation.*

We believe sumifilam [sic] improves brain health by reverting altered FLNA back to its native, healthy conformation, thus countering the downstream toxic effects of altered FLNA. *We have generated and published experimental and clinical evidence of improved brain health with sumifilam [sic].* Importantly, sumifilam [sic] is not dependent

on clearing amyloid from the brain. Since sumifilam [sic] has a unique mechanism of action, we believe its potential therapeutic effects may be additive or synergistic with that of other therapeutic candidates aiming to treat neurodegeneration.

***Sumifilam [sic] has demonstrated a multitude of beneficial effects in animal models of disease, including normalizing neurotransmission, decreasing neuroinflammation, suppressing neurodegeneration, and restoring memory and cognition.***

\* \* \*

In 2019, we completed a small, first-in-patient, clinical-proof-of-concept, open-label Phase 2a study of sumifilam [sic] in the U.S., with substantial support from the *National Institute on Aging* (“NIA”), a division of NIH. Drug was safe and well-tolerated in this study. ***Treatment with sumifilam [sic] for 28 days significantly improved key biomarkers of Alzheimer’s pathology, neurodegeneration and neuroinflammation ( $p<0.001$ ).*** Biomarkers effects were seen in all patients in both cerebrospinal fluid (“CSF”) and plasma.

\* \* \*

On September 14, 2020, we reported positive Phase 2b clinical study results. Drug was safe and well-tolerated in this study. ***Sumifilam [sic] significantly ( $P<0.05$ ) improved an entire panel of validated biomarkers of disease in patients with Alzheimer’s disease compared to a placebo group.*** In addition, ***Alzheimer’s patients treated with sumifilam [sic] showed directional improvements in validated tests of episodic memory and spatial working memory, versus patients on placebo*** (Effect Sizes 46-17%). Cognitive improvements correlated most strongly ( $R^2=0.5$ ) with decreases in levels of P-tau181 in CSF. The study achieved a 98% response rate, defined as the proportion of study participants taking sumifilam [sic] who showed improvements in biomarkers. ***Importantly, we believe these data are consistent with prior clinical and preclinical results, the drug’s mechanism of action and over 10 years of basic research.***

287. The statements made above in ¶¶269-286 were false and misleading when made because Defendants failed to disclose the following material facts:

(a) That Cassava’s foundational pre-clinical and clinical research, which provided the basis for the continued development for simufilam as a treatment for Alzheimer’s disease, including by supporting Cassava’s IND application for simufilam to the FDA, contained manipulated, duplicated, and scientifically improbable data, rendering it unreliable, including that:



(i) The 2008 manuscript “High-Affinity Naloxone Binding to Filamin A Prevents Mu Opioid Receptor-Gs Coupling Underlying Opioid Tolerance and Dependence,” *PLOS ONE* 3:e1554 (2008), a foundational paper funded by Pain Therapeutics and authored by Drs. Burns and Wang, contained manipulated data, including spliced and duplicated images;

(ii) The 2012 manuscript “Reducing amyloid-related Alzheimer’s disease pathogenesis by a small molecule targeting filamin A,” *The Journal of Neuroscience*, 32:9773–9784 (2012), a foundational paper funded by Pain Therapeutics and authored by Drs. Burns and Wang, contained manipulated data, including duplicated images, and relied on experiments that could not have been conducted as described;

(iii) The 2017 manuscript “PTI-125 Binds and Reverses an Altered Conformation of Filamin A to Reduce Alzheimer’s Disease Pathogenesis,” *Neurobiology of Aging*; 55:99-114 (2017), a foundational paper funded by Pain Therapeutics and authored by Drs. Burns and Wang, contained manipulated data, relied on a methodology for experimenting on human brain tissue that defied logic, and relied on experiments that could not have been conducted as described;

(iv) The 2020 manuscript “PTI-125 Reduces Biomarkers of Alzheimer’s Disease in Patients,” *Journal of Prevention of Alzheimer’s Disease* 7:256-264 (2020), a foundational paper reporting Cassava’s Phase 2a clinical trial results authored by Drs. Wang, Burns, Friedmann, and Mr. Barbier, contained: (i) manipulated images; and (ii) anomalous baseline measurements for three “key” biomarkers so far outside expectations and inconsistent compared to published studies as to evidence lab errors or manipulation, not scientifically valid results.

(b) That the two principal Cassava scientists developing simuflam as a treatment for Alzheimer’s disease, Drs. Burns and Wang, have a longstanding 15-year pattern of extensive data duplication and manipulation in scientific papers they co-authored, which, in totality, evidences systematic



data manipulation and misrepresentation. As detailed herein, these scientific papers included, but are not limited to:

(i) The 2005 manuscript “Ultra-low-dose naloxone suppresses opioid tolerance, dependence and associated changes in mu opioid receptor-G protein coupling and Gbetagamma signaling,” *Neuroscience* (2005), authored by Drs. Burns and Wang, which contained data, including duplicated and spliced images;

(ii) The 2006 manuscript “Gbetagamma that interacts with adenylyl cyclase in opioid tolerance originates from a Gs protein,” *Journal of Neurobiology* (2006), authored by Drs. Wang and Burns, which contained evidence of splicing;

(iii) The 2008 manuscript “High-Affinity Naloxone Binding to Filamin A Prevents Mu Opioid Receptor-Gs Coupling Underlying Opioid Tolerance and Dependence,” *PLOS ONE* 3:e1554 (2008), a foundational paper funded by Pain Therapeutics and authored by Drs. Burns and Wang, which was retracted by the publisher;

(iv) The 2008 manuscript “Oxycodone Plus Ultra-Low-Dose Naltrexone Attenuates Neuropathic Pain and Associated  $\mu$ -Opioid Receptor-Gs Coupling,” *The Journal of Pain* (2008), authored by Drs. Burns and Wang, which contained image anomalies indicative of manipulation;

(v) The 2009 manuscript “Naloxone’s Pentapeptide Binding Site on Filamin A Blocks Mu Opioid Receptor–Gs Coupling and CREB Activation of Acute Morphine,” *PLOS ONE* (2009), authored by Drs. Wang and Burns, which was retracted by the publisher;

(vi) The 2012 manuscript “Reducing amyloid-related Alzheimer’s disease pathogenesis by a small molecule targeting filamin A,” *The Journal of Neuroscience*, 32:9773–9784 (2012), a foundational paper funded by Pain Therapeutics and authored by Drs. Burns and Wang, which received an Expression of Concern from the publisher;

(vii) The 2017 manuscript “PTI-125 Binds and Reverses an Altered Conformation of Filamin A to Reduce Alzheimer’s Disease Pathogenesis,” *Neurobiology of Aging*; 55:99-114 (2017), a foundational paper funded by Pain Therapeutics and authored by Drs. Burns and Wang, which received an Expression of Concern from the publisher; and

(viii) The 2020 manuscript “PTI-125 Reduces Biomarkers of Alzheimer’s Disease in Patients,” *Journal of Prevention of Alzheimer’s Disease* 7;256-264 (2020), a foundational paper reporting Cassava’s Phase 2a clinical trial results authored by Drs. Wang, Burns, Friedmann, and Mr. Barbier;

(c) That the Phase 2a results, including those published in the 2020 paper authored by Drs. Wang, Burns, Friedmann, and Mr. Barbier in the *Journal of Prevention of Alzheimer’s Disease* 7;256-264 (2020), “PTI-125 Reduces Biomarkers of Alzheimer’s Disease in Patients,” and in Cassava’s presentation at the 12th International Conference on CTAD on December 5, 2019, contained: (i) manipulated images; and (ii) anomalous baseline measurements for three “key” biomarkers, pTau-181, TNF- $\alpha$ , and IL-1 $\beta$ , so far outside expectations and inconsistent compared to published studies as to evidence gross lab errors or manipulation, not scientifically valid results;

(d) That Cassava’s “key” biomarker results from the “final” Phase 2b reanalysis included anomalous data from three tested biomarkers (CSF/plasma albumin, IL-6, and sTREM2) so far outside expectations and inconsistent compared to published studies as to evidence gross lab errors or manipulation, not scientifically valid results, despite having previously discarded the initial Phase 2b trial results and conducted the reanalysis on the basis that the initial results, which did not support simufilam’s continued commercial development, were themselves purportedly “anomalous”;

(e) That Cassava’s “key” Spatial Memory test results from the “final” Phase 2b reanalysis, including as presented in its Conference on Clinical Trials on Alzheimer’s Disease: (i) were incorrect and misstated the results so that the 100 mg group reflects a “better” result than the 50 mg group,

when in fact the 50 mg result is -3.35 and the 100 mg result is -2.31 (lower score is considered better), not -1.65 for the 50 mg group and -3.35 for the 100 mg group as disclosed; and (ii) the purported “effect” of simufilam in the dosage groups is compromised by inequivalent baseline measurements, as seven individuals were removed from the baseline Spatial Working Memory test in the 100 mg and 50 mg dose groups;

(f) That Cassava’s “final” Phase 2b results from the “re-do” were not conducted by an “outside” lab, but rather by Dr. Wang, who is: (i) a paid Cassava consultant with numerous financial interests in simufilam’s commercial development and Cassava’s stock price; (ii) a member of Cassava’s scientific advisory board; and (iii) one of two principal scientists developing simufilam “in house” at Cassava;

(g) That, as a result of the foregoing, there was a reasonable likelihood that Cassava would face regulatory scrutiny in connection with the development of simufilam; and

(h) That, as a result of the foregoing, Defendants’ positive statements about the Company’s business, operations, and prospects were materially misleading and/or lacked a reasonable basis.

## **B. Cassava’s November 13, 2020 Public Offering**

288. A month after Cassava announced the results of its Phase 2b reanalysis, which sent the Company’s stock price soaring over 100% higher, Cassava took advantage of the increase to sell 9,375,000 shares of common stock for \$75 million in an underwritten public offering at a price of \$8.00 per share on November 13, 2020.

## **C. Statements Reporting the Results of Cassava’s Open Label Study Interim Analysis and Ongoing Development Program**

289. On February 2, 2021, the Company announced the results of an interim analysis from an open-label study extension of its Phase 2b trial in a press release entitled “Cassava Sciences’ Simufilam

Improves Cognition and Behavior in Alzheimer’s Disease in Interim Analysis of Open-label Study,” which was reviewed and approved by Barbier, Friedmann, and Schoen. The press release stated, in relevant part:

– Results Support Advancing Simufilam into Phase 3 Clinical Program

... Cassava Sciences, Inc. today announced results of an interim analysis from an open-label study of simufilam, its lead drug candidate for the treatment of Alzheimer’s disease. Patients’ cognition and behavior scores both improved following six months of simufilam treatment, with no safety issues.

\* \* \*

***“Today’s data once again suggests simufilam could be a transformative, novel therapeutic,” added Nadav Friedmann, PhD, MD, Chief Medical Officer. “It appears the drug’s unique mechanism of action has potential to provide a treatment benefit following 6 months of dosing.”***

\* \* \*

***Cassava Sciences believes today’s data and prior clinical results support advancing simufilam into a Phase 3 clinical program in Alzheimer’s disease.*** Initiation of a Phase 3 trial remains on schedule for 2nd half 2021.

\* \* \*

Simufilam is a proprietary, small molecule (oral) drug that restores the normal shape and function of altered filamin A (FLNA), a scaffolding protein, in the brain. Altered FLNA in the brain disrupts the normal function of neurons, leading to Alzheimer’s pathology, neurodegeneration and neuroinflammation. ***The underlying science for simufilam is published in peer-reviewed journals, including Journal of Neuroscience, Neurobiology of Aging, Journal of Biological Chemistry, Neuroimmunology and Neuroinflammation and Journal of Prevention of Alzheimer’s Disease.***<sup>7</sup>

290. Following the Company’s February 2, 2021 announcement, the price per share of the Company’s common stock skyrocketed, from \$22.99 per share at the close of trading on February 1, 2021 to \$55.44 per share at market close on February 2, 2021. At market close on February 3, 2021, the price of

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<sup>7</sup> This statement is repeated in a March 23, 2021 press release filed with the SEC on Form 8-K on March 23, 2021, a July 26, 2021 press release, and a July 29, 2021 press release and August 3, 2021 press release, filed with the SEC on Form 8-K on August 3, 2021, which were reviewed and approved by Barbier, Friedmann and Schoen. They are alleged to be false and misleading in each instance for the reasons provided in ¶295.

the Company’s common stock was \$87.95 per share, an increase of approximately 383% from its February 1, 2021 price.

291. On February 8, 2021, Cassava filed a Form 8-K with the SEC, which was reviewed and approved by Barbier and Schoen, attaching a press release entitled “Cassava Sciences Announces Significant Program Progress and Expected Key Milestones in 2021 for Its Clinical Program in Alzheimer’s Disease,” and a corporate presentation, dated February 2021.

292. The presentation, authored by Drs. Burns, Friedmann, and Jim Kupiec, Cassava’s recently appointed Chief Clinical Development Officer, reiterated the “[*key drivers of our clinical development program*]” which included, among other things:

- “*A decade of research in basic biology*”;
- “*Published pre-clinical results*”;
- “*Unprecedented CSF biomarker data*”; and
- “*Phase 2b clinical results.*”

293. The presentation continued: “*Published preclinical data and mechanism of action studies support simufilam’s potential as a disease-modifying drug for AD that also provides symptomatic improvement.*”

294. On a slide entitled “Clinical Development” the presentation stated:

2019: *positive results on CSF biomarkers of disease in an open-label Phase 2a study of simufilam in AD patients.*

2020: *positive results on CSF biomarkers of disease in a double-blind, randomized, placebo-controlled Phase 2b study of simufilam in AD patients.*

The specific Phase 2b clinical results for the CSF biomarkers and spatial working memory test were also included in a “Phase 2b Summary of Results – CSF Biomarker” and “Cognition” sections, which presented data on the albumin, IL-6 and sTREM2 biomarkers and spatial working memory, among others. The presentation stated “*Biomarkers of Neuroinflammation Decreased Significantly in Both Drug Groups*”

for IL-6 and sTREM2, and, regarding albumin, “*Phase 2b Results – Improved Blood-brain Barrier Integrity.*” The presentation further reproduced the spatial working memory data shown in ¶274.

Regarding the Phase 2b results, the presentation concluded:

- *Simufilam improved a panel of validated biomarkers of disease pathology, neuroinflammation and BBB integrity.*

\* \* \*

- *Phase 2b data replicate prior clinical results and are consistent with published preclinical data and mechanism of action studies.*

295. The statements made above in ¶¶289-294 were false and misleading when made for the same reasons provided in ¶287.

#### **D. February 10, 2021 Stock Offering**

296. A little over a week after Cassava’s February 2, 2021 press release, which caused the Company’s stock to rise approximately 383%, Cassava again cashed in on its increased share price. In a February 10, 2021 direct registered stock offering, Cassava raised approximately \$200 million, selling 4,081,633 shares of the Company’s common stock priced at \$49 per share.

#### **E. Defendants Continue to Tout Cassava’s Pre-Clinical Research and Clinical Trial Results**

297. On February 22, 2021, Cassava issued a press release entitled “Cassava Sciences Announces Positive End-of-Phase 2 Meeting with FDA and Outlines Pivotal Phase 3 Program for Simufilam in Alzheimer’s Disease.” It stated, in relevant part:

**- Two Upcoming Phase 3 Studies and a Previously Completed Phase 2 Program Support a [NDA] Filing for Simufilam in Alzheimer’s disease -**

**- Agreement Reached to Use ADAS-Cog as Co-Primary Efficacy Endpoint -**

**- Pivotal Phase 3 Program Remains On-track to be Initiated 2nd Half 2021 -**

... Cassava Sciences, Inc., a biotechnology company developing product candidates for Alzheimer’s disease, today announced the successful completion of an End-of-Phase 2 (EOP2) meeting with the [FDA] for simufilam, its lead drug candidate for the treatment of Alzheimer’s disease. Official EOP2 meeting minutes indicate FDA and

Cassava Sciences agree on key elements of a pivotal Phase 3 clinical program in support of a [NDA] filing for simufilam in Alzheimer's disease. Agreements reached during the EOP2 meeting show a clear path forward for advancing simufilam into Phase 3 studies in the second half of 2021.

"For over 10 years we've been doing basic research and early drug development with simufilam," said Remi Barbier, President & CEO. "We are excited to finally advance simufilam into pivotal Phase 3 clinical studies in people with Alzheimer's disease. ***We believe the underlying science is solid, the drug appears safe and the clinical roadmap makes sense. We've crossed the Rubicon.***"

"We appreciate the valuable guidance and flexibility FDA has provided," added Jim Kupiec, MD, Cassava Sciences' Chief Clinical Development Officer. "We look forward to continuing a collaborative dialogue throughout the pivotal Phase 3 clinical development program."

Simufilam is a novel drug, discovered at Cassava Sciences, that targets both neuroinflammation and neurodegeneration. ***The EOP2 meeting discussion was supported by years of scientific and clinical data, including positive results from a previously completed Phase 2 clinical program with simufilam in Alzheimer's disease. In a double-blind, randomized, placebo-controlled Phase 2b study, simufilam demonstrated robust effects on primary and secondary outcome measures, with no safety issues.*** Recently, the Company announced that simufilam improved cognition in subjects with Alzheimer's disease in a 6-month interim analysis of an open-label study, with no safety issues.

298. On March 9, 2021, Cassava participated in the H.C. Wainwright Annual Global Life Sciences Virtual Conference. During Cassava's presentation at the conference, Barbier stated:

I think, the key take-home message for around Cassava Sciences is that simufilam is a Phase 3 ready asset in 2021. There are many, many drivers of our clinical development plan, ***but suffice to say that it is our scientific plan and our clinical plan is based on years and years of research around basic biology and specifically the basic biology of filamin A***, a protein that we'll talk more about.

299. Barbier continued: "Unlike many drugs, simufilam has a dual mechanism of action, meaning that it – it is intended to both reduce neurodegeneration as well as reduce neuroinflammation. ***And we have a lot of published data and around both the preclinical data the clinical data and mechanism of action for simufilam.***"

300. Barbier also continued to praise that simufilam's mechanism of action was "well described and published":



One of our contribution [sic] to the field, to the Alzheimer's field is that the Alzheimer's brain in fact carries an altered form of filamin A. And what we are saying is that, it is the altered form, the altered filamin A protein that is critical to the toxicity of amyloid beta. *How that happens again rather complicated, there's a very specific and well described and published mechanism of action, but the take home message here is that simufilam binds the altered form of filament A, restores its proper shape and function and disables amyloid beta from signaling via all these different receptors, hence reducing neurodegeneration and neuroinflammation.*

301. Barbier concluded:

So in conclusion to [sic] *Phase 2b study shows that simufilam did improve an entire panel of biomarkers of disease pathology, inflammation and blood-brain barrier integrity and at the Phase 2b data do replicate prior clinical results, and more importantly, are consistent with the science, consistent with the mechanism of action studies.*

302. Then the Company filed a Form 8-K with the SEC on March 23, 2021, which was reviewed and approved by Barbier and Schoen, attaching a press release entitled "Cassava Sciences Announces Full-year 2020 Financial Results and Business Highlights." The press release stated, in relevant part:

"In Q1 2021 we announced that our lead drug candidate, simufilam, improved cognition scores in 50 patients with Alzheimer's disease who completed at least 6 months of open-label treatment," said Remi Barbier, President & CEO. "In mid-2021, we look forward to announcing cognition scores in patients who'll have completed at least 12 months of open-label treatment with simufilam. To our knowledge, no drug has stabilized, much less improved, cognition scores over 12 months in patients with Alzheimer's disease. For this reason, I feel there is a sense of anticipation around the upcoming release of 12-month clinical data from our open-label study, as well as our plans to conduct a pivotal Phase 3 program with simufilam in the second half of 2021. *With solid science, the right people in place, cash in the bank and a clinical roadmap that makes sense, I think Cassava Sciences is positioned to becoming a premier organization to serve patients with Alzheimer's disease.*"<sup>8</sup>

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<sup>8</sup> Notably, following the news of the Citizen Petition and the follow-on investigations detailed herein, patient enrollment for Cassava's now ongoing Phase 3 clinical trials have lagged. An April 5, 2022 article in STAT news entitled "Troubles mount for Cassava Sciences, as patient enrollment lags for Alzheimer's drug studies," reported that "Cassava Sciences conceded Tuesday that only a relative handful of patients with Alzheimer's have been enrolled in its late-stage clinical trials – a sign that ongoing investigations over the credibility of its experimental drug simufilam have made physicians and patients wary."

303. Also on March 23, 2021, Cassava filed its annual report for 2020 on Form 10-K with the SEC. The 2020 Form 10-K was signed by Defendants Barbier, Schoen and Friedmann.

304. The 2020 Form 10-K stated, in relevant part:

Our lead therapeutic product candidate, simufilam, is a proprietary small molecule (oral) drug. Simufilam targets an altered form of a protein called filamin A (FLNA) in the Alzheimer's brain. ***Published studies have demonstrated that the altered form of FLNA causes neuronal dysfunction, neuronal degeneration and neuroinflammation.***<sup>9</sup>

We believe simufilam improves brain health by reverting altered FLNA back to its native, healthy conformation, thus countering the downstream toxic effects of altered FLNA. ***We have generated and published experimental and clinical evidence of improved brain health with simufilam.*** Importantly, simufilam is not dependent on clearing amyloid from the brain. Since simufilam has a unique mechanism of action, we believe its potential therapeutic effects may be additive or synergistic with that of other therapeutic candidates aiming to treat neurodegeneration.<sup>10</sup>

***Simufilam has demonstrated a multitude of beneficial effects in animal models of disease, including normalizing neurotransmission, decreasing neuroinflammation, suppressing neurodegeneration, and restoring memory and cognition.***<sup>11</sup>

In 2019, we completed a small, first-in-patient, clinical-proof-of-concept, open-label **Phase 2a study** of simufilam in the U.S., with substantial support from the *National Institute on Aging* (NIA), a division of the NIH. ***Treatment with simufilam for 28 days significantly improved key biomarkers of Alzheimer's pathology, neurodegeneration and neuroinflammation (p<0.001). Biomarkers effects were seen in all patients in both cerebrospinal fluid (CSF) and plasma.***<sup>12</sup>

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<sup>9</sup> This statement was repeated in Cassava's Form 10-Q for the first and second quarters of 2021, which were signed by Barbier and Schoen, and filed with the SEC on April 29, 2021 and August 4, 2021, respectively.

<sup>10</sup> This statement was repeated in Cassava's Form 10-Q for the first and second quarters of 2021, which were signed by Barbier and Schoen, and filed with the SEC on April 29, 2021 and August 4, 2021, respectively.

<sup>11</sup> This statement was repeated in Cassava's Form 10-Q for the first and second quarters of 2021, which were signed by Barbier and Schoen, and filed with the SEC on April 29, 2021 and August 4, 2021, respectively.

<sup>12</sup> This statement was repeated in Cassava's Form 10-Q for the first and second quarters of 2021, which were signed by Barbier and Schoen, and filed with the SEC on April 29, 2021 and August 4, 2021, respectively.

In September 2020, we announced final results of a **Phase 2b study** with simufilam in Alzheimer's disease. *In this clinical study funded by the NIH, Alzheimer's patients treated with 50 mg or 100 mg of simufilam twice-daily for 28 days showed statistically significant ( $p < 0.05$ ) improvements in CSF biomarkers of disease pathology, neurodegeneration and neuroinflammation, versus Alzheimer's patients who took placebo. In addition, Alzheimer's patients treated with simufilam showed improvements in validated tests of episodic memory and spatial working memory, versus patients on placebo (Effect Size 17-46%).* Cognitive improvements correlated most strongly ( $R^2 = 0.5$ ) with decreases in levels of Ptau181.<sup>13</sup>

Using scientific insight and advanced techniques in molecular biochemistry, bioinformatics and imaging, we have elucidated this protein dysfunction. *Through this work, we have produced experimental evidence that altered FLNA plays a critical role in Alzheimer's disease.* We engineered a family of high-affinity, small molecules to target this structurally altered protein and restore its normal shape and function. This family of small molecules, including our lead therapeutic candidate, simufilam, was designed in-house and characterized by our academic collaborators.

\* \* \*

FLNA is a scaffolding protein widely found throughout the body. A healthy scaffolding protein brings multiple proteins together, initiating their interaction. However, an altered form of FLNA protein is found in the Alzheimer's brain. *Our experimental evidence shows that altered FLNA protein contribute to Alzheimer's disease by disrupting the normal function of neurons, leading to neurodegeneration and brain inflammation.* Our product candidate, simufilam, aims to counter the altered and toxic form of FLNA in the brain, thus restoring the normal function of this critical protein. Our novel science is based on stabilizing – but not removing – a critical protein in the brain.

\* \* \*

*Our science is published in multiple peer-reviewed journals. In addition, our research has been supported by NIH under multiple research grant awards. Each grant was awarded following an in-depth, peer-reviewed evaluation of our approach for scientific and technical merit by a panel of outside experts in the field.* Strong, long-term support from NIH has allowed us to advance our two product candidates for neurodegeneration, simufilam and SavaDx, into clinical development.

*We have generated and published experimental evidence of improved brain health by restoring altered FLNA with simufilam, our lead therapeutic product candidate.* Simufilam is a proprietary small molecule drug that represents an entirely new scientific approach to treat neurodegeneration. *Published studies have demonstrated that simufilam targets an altered form of a protein called FLNA that is pervasive in the*

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<sup>13</sup> This statement was repeated in Cassava's Form 10-Q for the first and second quarters of 2021, which were signed by Barbier and Schoen, and filed with the SEC on April 29, 2021 and August 4, 2021, respectively.

***Alzheimer's brain.*** Altered FLNA causes neuronal dysfunction, neuronal degeneration and neuroinflammation. We believe our drug candidate, simufilam, improves brain health by reverting altered FLNA back to its native, healthy conformation, thus countering downstream toxic effects of altered FLNA. Importantly, simufilam is not dependent on clearing amyloid from the brain. The following is a summary profile of simufilam's drug development program.

***Over the past ten years, we successfully conducted basic research, in vitro studies and preclinical studies in support of an [IND] submission to FDA for simufilam, including requisite studies around safety pharmacology, toxicology, genotoxicity and bioanalytical methods.*** In 2017 we filed an IND with FDA for simufilam.

\* \* \*

Given the absence of any observable dose-limiting effects in healthy adults in a Phase 1 study, ***a strong scientific rationale, and multiple peer-reviewed publications and research grant awards, we believe this program demonstrated favorable proof-of-principle for the development of simufilam in Alzheimer's disease.***

A key objective of our Phase 2a study was to measure levels of CSF biomarkers in the brain. ***Key results of this study include*** (Figure 1):

- Total tau (T-tau) decreased 20% (p<0.001)
- ***Phosphorylated tau (P-tau) decreased 34% (p<0.0001)***
- Neurofilament light chain (NfL), a marker for neurodegeneration, decreased 22% (p<0.0001)
- Neurogranin, a marker for cognitive decline, decreased 32% (p<0.0001)
- Neuroinflammatory marker YKL-40, an indicator of microglial activation, decreased 9% (p<0.0001)
- Proinflammatory Interleukin 6 (IL-6) decreased 14% (p<0.0001)
- ***Proinflammatory Interleukin 1 beta (IL-1 $\beta$ ) decreased 11% (p<0.0001)***
- ***Proinflammatory Tumor Necrosis Factor alpha (TNF $\alpha$ ) decreased 5% (p<0.001)***

\* \* \*

***Consistent with over 10 years of basic research and pre-clinical data, we believe our Phase 2a study showed clinical evidence of simufilam's mechanism of action and drug-target engagement, including:***

- ***Improvements in biomarkers of Alzheimer's disease in CSF, plasma and lymphocytes;***
- ***Consistency across biomarker improvements in CSF, plasma, and lymphocytes . . . .***

\* \* \*

In February 2020, our Phase 2a study was published in *The Journal of Prevention of Alzheimer's Disease* (JPAD), a technical journal for the research community. ***This peer-reviewed publication highlighted that biomarkers of Alzheimer's disease pathology (P-tau, total tau and A $\beta$ 42), neurodegeneration (NfL and neurogranin) and neuroinflammation (YKL-40, IL-6, IL-1 $\beta$  and TNF $\alpha$ ) improved significantly after 28 days of treatment with simufilam.***

\* \* \*

In May 2020, we announced that an outside lab with whom we had no prior work experience had generated an initial bioanalysis of CSF samples from our Phase 2b study. The data set from the initial bioanalysis showed unnaturally high variability and other problems, such as no correlation among changes in levels of biomarkers over 28 days, even in the placebo group, and different biomarkers of disease moving in opposite directions in the same patient. Importantly, we later observed no statistical correlation between levels of simufilam in plasma and CSF, further indicating an invalid analysis. ***Overall, we believe data from the initial [Phase 2b] bioanalysis can be interpreted as anomalous and highly improbable. With its validity in question, the initial bioanalysis serves no useful purpose. Backup CSF samples were subsequently sent to a second outside lab for bioanalysis.*** All bioanalyses were conducted under blinded conditions to eliminate any possibility of bias.

On September 14, 2020, we reported final positive Phase 2b clinical study results. Drug was safe and well-tolerated in this study. ***Simufilam significantly (P<0.05) improved an entire panel of validated biomarkers of disease in patients with Alzheimer's disease compared to a placebo group. In addition, Alzheimer's patients treated with simufilam showed directional improvements in validated tests of episodic memory and spatial working memory, versus patients on placebo*** (Effect Sizes 46-17%). Cognitive improvements correlated most strongly (R=0.5) with decreases in levels of Ptau181 in CSF. The study achieved a 98% response rate, defined as the proportion of study participants taking simufilam who showed improvements in biomarkers. We later observed a direct correlation between levels of simufilam in plasma and CSF, which provides strong evidence of a valid analysis. ***Importantly, we believe these data are consistent with prior clinical and preclinical results, the drug's mechanism of action and over 10 years of basic research.***

\* \* \*

***Key biomarker results include the following*** (all p-values versus placebo) (**Figure 3**):

\* \* \*

- Proinflammatory IL-6 (Interleukin 6) is produced in response to tissue stress and injury.
- *IL-6 decreased 10% ( $p<0.01$ ) for patients in the 50 mg drug group.*
- *IL-6 decreased 11% ( $p<0.01$ ) for patients in the 100 mg drug group.*

\* \* \*

- sTREM2 is a neuroinflammation biomarker that has commanded substantial recent attention from researchers for its role in Alzheimer’s disease and frontotemporal dementia.
- *sTREM2 decreased 43% ( $p<0.01$ ) for patients in the 50 mg drug group.*
- *sTREM2 decreased 46% ( $P<0.01$ ) for patients in the 100 mg drug group.*

\* \* \*

- *Simufilam Improved the Albumin Ratio, a Test of Blood-brain Barrier (BBB) Permeability . . . .*

The 10-K further reported “[*k*]ey *cognition results*,” including that “[s]patial memory improved by -1.6 (lower score is better) for Alzheimer’s patients in the 50 mg drug group, versus -0.4 for patients on placebo” and “[s]patial memory improved by -3.3 (lower score is better) for Alzheimer’s patients in the 100 mg drug group, versus -0.4 for patients on placebo.”





305. The statements made above in ¶¶297-304 were false and misleading when made for the same reasons provided in ¶287.

**F. April 28, 2021 B. Riley Neuroscience Conference**

306. At the April 28, 2021 B. Riley Neuroscience Conference, Barbier stated:

*And that is why, when we look at our Phase 2 results -- Phase 2b. And you look at our Phase 2 results. Phase 2b – they both Phase 2a, Phase 2b, what we see that has never been seen for is a massive reduction in biomarkers of neuroinflammation, biomarkers of neurodegeneration and other indications of disease.*

307. Barbier then extolled the “consistency” of Cassava’s pre-clinical and clinical data, stating:

*But again, connecting the dots from an academic thesis to a drug that works for the average patient. I haven’t seen that too often. **Hear what we really like, one of the things we like about the program. And perhaps really where we get our confidence in the Phase 3 possibilities. Is that all the dots connect. Again, all the way from basic biology to CSF markers to mechanism of actions, animals and now cognition.***

308. The statements made above in ¶¶306-307 were false and misleading when made for the same reasons provided in ¶287.

**G. June 22, 2021 Raymond James Human Health Innovation Conference**

309. During a presentation at the June 22, 2021 Raymond James Human Health Innovation Conference, Barbier stated:



*The preclinical data and the mechanism of action studies in support of simufilam are published in a number of peer-reviewed publications. And we think that these publications and certainly our clinical data point to simufilam's potential as a drug-modifying drug -- disease-modifying drug, pardon me, for Alzheimer's that also provides symptomatic improvement.*

310. Barbier continued:

At this point, we can say that simufilam appeared to enhance cognition, and that those enhancements in fact correlate at some level with P-tau181. *But at a very high strategic level, what we show here is that the Phase 2b data replicate earlier clinical results and are consistent with mechanism of action studies and published preclinical data.*

311. The statements made above in ¶¶309-310 were false and misleading when made for the same reasons provided in ¶287.

#### **H. July 26, 2021 Press Release**

312. On July 26, 2021, the Company issued a press release titled "Cassava Sciences Announces Positive Data with SavaDx from a Randomized Controlled Phase 2b Study of Simufilam[.]" It stated, in relevant part:

*Cassava Sciences, Inc. (Nasdaq: SAVA) today announced positive clinical data with SavaDx, an investigational diagnostic/biomarker to detect Alzheimer's disease with a simple blood test. SavaDx was used to measure plasma levels of altered filamin A before and after simufilam treatment in patients with Alzheimer's disease. In this Phase 2b randomized, controlled trial sponsored by the [NIH], simufilam significantly reduced plasma levels of altered filamin A in Alzheimer's patients treated for 28 days. Plasma levels of p-tau181 also dropped significantly in these same patients.*

Simufilam 100 mg and 50 mg reduced plasma levels of altered filamin A by 48% (p=0.003) and 44% (p=0.02) respectively, versus placebo. Additionally, *simufilam 100 mg and 50 mg reduced plasma levels of p-tau181 by 17% (p=0.01) and 15% (p=0.02) respectively, versus placebo.* Plasma p-tau181 is a biomarker that is known to be elevated in Alzheimer's disease.

"We believe altered filamin A is a major culprit in Alzheimer's disease," said Remi Barbier, President & CEO. "Before simufilam treatment, SavaDx detected high plasma levels of altered filamin A in patients. *After simufilam treatment, levels dropped significantly. We believe these data provide clear evidence that simufilam binds to and engages its intended target to produce treatment effects.*"

313. The press release further stated:

Scientists for Cassava Sciences will show a poster presentation titled, ‘SavaDx, a Novel Plasma Biomarker to Detect Alzheimer’s Disease, Confirms Mechanism of Action of Simufilam’ at the AAIC in Denver, CO and virtually. Cassava Sciences’ AAIC poster presentation with SavaDx can be accessed on the ‘Investors’ page of the Company’s website: <https://www.CassavaSciences.com>.

314. The poster presentation, entitled “SavaDx, a Novel Plasma Biomarker to Detect Alzheimer’s Disease, Confirms Mechanism of Action of Simufilam,” listed the names of Drs. Burns and Wang, along with Zhe Pei from the CUNY, Qiang Xu from Abilene Christian University, Lynn Brunelle from Quanterix, and George Thornton from Cassava, and included the **Figures 4 and 5** pictured at ¶218.

315. The statements made above in ¶¶312-314 were false and misleading when made because Defendants failed to disclose the information provided in ¶287, and:

(a) That biomarker results for plasma P-tau181 improperly excluded data that, if included would have resulted in an approximately -3% reduction in the plasma P-tau181 biomarker for Alzheimer’s compared to placebo, a non-statistically significant change, not the “significant[],” -17% average reduction claimed by the Company;

(b) That Cassava’s AAIC poster presented falsified or manipulated “altered Filamin A” data, materially different from the raw Western blot data underlying the experiments obtained from Dr. Wang’s email pursuant to a FOIL request, which is further supported by the improbable location of filamin A in the middle of the Western blot panels included in the AAIC poster, as high molecular weight proteins such as filamin A should appear near the top of the Western blot image.

## **VII. THE TRUTH IS PARTIALLY REVEALED AS DEFENDANTS CONTINUE TO MISLEAD**

316. On August 25, 2021, before the market opened, the Company issued a public statement, “Cassava Sciences Responds to Allegations,” in which it responded to the Citizen Petition, which had been “posted on-line yesterday after market hours.” In its response, Cassava explicitly denied the Citizen Petition’s accusations, stating, “Cassava Sciences believes the claims made in this post regarding scientific

integrity are false and misleading,” and further stated that the Company “stands behind its science, its scientists and its scientific collaborators, and is responding to ensure the facts are known and respected.”

317. The rest of the release labeled various statements from the Citizen Petition as “fiction” and then proceed to set out the purported “fact,” according to Cassava. Specifically, it stated:

**Fiction:** *Biomarker data is generated by Cassava Sciences or its science collaborators and therefore are falsified.*

**Fact:** *Cassava Sciences’ plasma p-tau data from Alzheimer’s patients was generated by [Quanterix], an independent company, and presented at the recent Alzheimer’s Association International Conference[.]*

**Fiction:** Plasma p-tau for one individual Alzheimer’s patient increased by 235%, which was not shown in the scatterplot.

**Fact:** *This patient’s plasma p-tau increased by 38%, not 235%, as shown in a scatterplot.[.]*

**Fiction:** Tissue staining showing Abeta42 inside neurons shows treatment effects.

**Fact:** Yes, Abeta42 is indeed inside neurons prior to plaque formation.

**Fiction:** The author’s Citizen Petition to FDA dated August 18, 2021, is evidence of wrongdoing.

**Fact:** Five days after the Citizen’s Petition, Cassava Sciences announced it had reached an agreement with FDA on Special Protocol Assessments (SPA) for its Phase 3 studies of simufilam for the treatment of Alzheimer’s disease. The SPAs underscore alignment with FDA on key scientific, clinical and regulatory requirements of the Company’s Phase 3 program of simufilam in Alzheimer’s disease.[.] Furthermore, a Citizen’s Petition allows any party to raise safety/efficacy concerns with drugs the FDA is considering for approval, which is not the case for Cassava Sciences’ simufilam.[.]

**Fiction:** Extensive use of Western blot analysis is foundational to Cassava Sciences’ research and therefore suspicious.

**Fact:** Western blot analysis is foundational to the biotechnology industry[.]. Western blotting is a standard lab technique used world-wide to detect a protein of interest.

**Fiction:** Cassava Sciences’ Western blots data appear overexposed and highly processed, evidence of image manipulation.

**Fact:** High quality bands are supposed to look sharp[.]. Smudged bands can be evidence of inexperience, depending on levels of protein in the band.

**Fiction:** Western blots data are identical, more evidence of image manipulation.

**Fact:** The Western blots bands shown in the allegation are control bands. Control bands are supposed to be highly similar (since they show equal amounts of protein between lanes). Bands show clear differences when expanded. In addition, image manipulation of control bands makes no sense since these would not change the end data.

**Fiction:** “Halo” effects in certain bands indicate fraud.

**Fact:** A “Halo” effects in certain bands is a direct result of very dense dark loading control bands.[]

**Fiction:** Unusual looking bands on Western blots were pieced together from multiple sources.

**Fact:** Proteins can and do stick to the side of a lane and migrate that way, resulting in ‘candy-wrapper’ appearance or other fictional images.

**Fiction:** Femtomolar binding affinity is unusual and suspicious.

**Fact:** Femtomolar binding affinity is a fundamental property of simufilam and may account for its relative potency and safety.

**Fiction:** Post-mortem brain tissue that is dead for a decade is unreliable.

**Fact:** Because of the inaccessibility of the human brain and its unavailability for biopsy, translational medicine can rely on post-mortem tissue[]. In our case, human brain tissue was collected within 6 hours of death, flash-frozen and stored at -80 Centigrade. This is a standard procedure for pathologists. Such tissue processing is also used in cancer and other fields. Cassava Sciences is not aware of an industrywide ‘expiration date’ on human post-mortem brain tissue that is properly collected, processed and stored.

**Fiction:** Isoelectric focusing gels should not have crisp bands, which is evidence of fraud.

**Fact:** Quality isoelectric focusing gels often do have crisp bands[].

**Fiction:** Changes in the Y-maze test for transgenic mice could be interpreted as a decline in cognition.

**Fact:** A panel of independent, peer-reviewers believe these changes represent an improvement, along with significant improvements in two other behavior tests.

**Fiction:** High-affinity binding of naloxone for filamin A is suspicious.

**Fact:** Naloxone binds the same site on filamin A. Of course, it will have high affinity binding.

**Fiction:** Isoelectric focusing experiments indicate 100% of filamin A is in altered conformation in Alzheimer’s disease and is largely restored to correct conformation by simufilam.

**Fact:** Cassava Sciences agrees. This nicely describes the mechanism of action for simufilam.

318. On this news, the Company’s share price fell \$36.97 per share, or 32%, to close at \$80.86 per share on August 25, 2021, on unusually heavy trading volume. The Company’s stock price continued to trade down the next day, August 26, further falling to a close of \$70.85 per share, on sustained heavy trading volume of 25 million shares.

319. In addition, the statements made above in ¶317 were false and misleading when made because they failed to disclose:

(a) That Quanterix did not interpret the test results or prepare the charts presented by Cassava at the AAIC; and

(b) That the missing plasma p-tau data for the individual patient removed from the 100 mg dose group in Cassava’s AAIC presentation showed an increase of 150%, not 38%, as the Company claimed.

320. After reviewing Cassava’s August 25, 2021 response to the Citizen Petition, Dr. Bik wrote on her website: “The parts of the response dealing with the problematic Western blots *are not very convincing*.” “Rather than trying to dismiss the *valid* concerns with vague statements that ‘control bands are supposed to be highly similar’ and calling the concerns ‘fiction,’” she stated, “I would like to see the authors present high-quality scans of the uncropped Western blot films.” Barbier himself agreed, later stating in a September 3, 2021 “public statement,” that “[o]ne way to settle the discourse around Western blots might be to go back to the original films and images.”

321. But Barbier has never provided the original films and images to Dr. Bik or the public more generally to dispel these concerns, despite Cassava’s control over this data, which includes, according to Cassava’s 2020 Form 10-K, confidentiality agreements signed by the Company’s scientific collaborators and advisors to protect Cassava’s “proprietary information and the results of studies conducted at our request.”

322. In a November 23, 2021 *Fierce Biotech* article, entitled “Data manipulation expert Elisabeth Bik compares the tales of 2 accused biotechs: Cassava and Athira,” Dr. Bik offered an even more damning assessment of Cassava’s response, stating:

[Cassava] released this statement where is had like facts and fiction. Basically, they called all these allegations fiction, and then they had facts, and *some of these facts were clearly, in my opinion, fiction*, and it was *not written by a person who had any knowledge about molecular biology or about blots in general*. It was very dismissing of all the concerns, while, in my opinion, the *concerns had merit*.

Indeed, Dr. Bik had Tweeted on August 25, 2021, after seeing Cassava’s response: “Whoa. \$SAVA / @CassavaSciences response to (*legit*) allegations that Western blot bands look similar or spliced *raises even more concerns*.”

## VIII. THE TRUTH CONTINUES TO EMERGE

### A. August 27, 2021 Quanterix Response and Dr. Bik Blog Post Raise Additional Concerns

323. On August 27, 2021, before the market opened, Quanterix issued a statement that Quanterix did not interpret the Company’s clinical data or prepare the charts contained in Cassava’s July 26, 2021 AAIC presentation. Specifically, it stated:

Cassava previously engaged Quanterix’ Accelerator laboratory to perform sample testing based on blinded samples provided by Cassava. *Quanterix or its employees did not interpret the test results or prepare the data charts presented by Cassava at the Alzheimer’s Association International Conference (AAIC) in July 2021 or otherwise.*

324. The same day, Cassava responded to Quanterix’s statement, confirming that “Quanterix’[s] sole responsibility with regard to this clinical study was to perform sample testing, specifically, to measure levels of p-tau in plasma samples collected from study subjects.” The Company’s press release stated, in relevant part:

The Phase 2b clinical study was conducted by Cassava Sciences. Quanterix’ sole responsibility with regard to this clinical study was to perform sample testing, specifically, to measure levels of p-tau in plasma samples collected from study subjects.

“To ensure data integrity, it is standard industry practice to keep separate the people who generate the data from the people who analyze the data,” said Remi Barbier,

President & CEO. “That certainly was the case here. Anything different is a distortion of the facts.”

Quanterix’ sample testing was conducted entirely by its employees. Quanterix’ employees were blind to treatment group, i.e., they did not know which samples were from placebo, or simufilam-treated patients. Quanterix conducted sample testing, then sent raw data to Cassava Sciences for analysis of treatment effects. Eventually, Cassava Sciences presented these data in a poster presentation at the Alzheimer’s Association International Conference (AAIC) in July 2021. In keeping with scientific authorship guidelines, prior to submitting the abstract to AAIC, Cassava Sciences received permission from Quanterix to include its lab personnel in the author list.

325. In addition to the Quanterix press release, Cantor Fitzgerald suspended its coverage of Cassava and their \$109 price target in an August 27, 2021 report entitled “Simufilam Diligence Challenge Tough to Reconcile; Suspending Rating and PT.” The report stated: “[I]t will not be possible to properly diligence these allegations” made by a law firm in the citizen’s petition filed with the [FDA] “without non-public records from [Cassava] as well as raw data, which we do not have access to.”

326. Further, Dr. Bik posted on her blog that day that she “took a look at the problematic photos included in the [Citizen Petition] report, and *agree[d] with most of those concerns*,” and “also found some additional problems.” She reviewed “[o]ther papers with image concerns,” stating “[a]t least five other articles from the Wang lab at CUNY appear to show image concerns as well,” implicating Pain Therapeutics and Drs. Burns and Wang. As discussed in ¶¶241-244, she also found additional evidence of data manipulation in **Figure 3A** of Cassava’s 2020 *JPAD* paper.

327. On this news, the Company’s share price fell \$12.51 per share, or 17.6%, to close at \$58.34 per share on August 27, 2021, on unusually heavy trading volume.

## **B. August 30, 2021 Supplement to the Citizen Petition Raises New Concerns**

328. A supplement to the Citizen Petition, dated August 30, 2021, identified “new errors and anomalies that strongly suggest scientific misconduct in their reports about both preclinical and clinical data.” The petition supplement reported that the poster Cassava presented at the AAIC on July 26, 2021 contained data discrepancies in **Figures 4 and 5**, including a missing data point in **Figure 4** in the 100 mg



treatment group that changed the p-value from the Company's reported value of ~0.01 to a *non-significant* p-value of 0.08. According to the petition supplement, when the values were recalculated using paired t-tests accounting for that switch, the p-values for the 50 mg and 100 mg treatment groups become larger (0.034 and 0.15, respectively), and because the study evaluated multiple biomarkers, *neither of these groups would be considered statistically different from placebo* when accounting for multiple comparisons.

329. That same day, Dr. Bik also published a post on her blog stating that she “*agree[d] with those concerns*” raised in the Citizen Petition concerning the data in **Figures 4 and 5** of the AAIC poster. And she similarly found that if the 150% outlier data point from the poster “had been included in the 100 mg treatment group,” as it should have been, instead of the placebo group in the poster, “the average change-from-baseline would change from -17% to around -3%, which is a *much less spectacular reduction* of plasma P-tau181 levels than claimed by the company.”

330. On this news, Cassava's stock price fell 8.7% to close at \$53.26 per share.

**C. September 3, 2021 “Cassava Sciences Releases a Public Statement Regarding Recent Allegations”**

331. On September 3, 2021, Cassava issued a press release “Cassava Sciences Releases a Public Statement Regarding Recent Allegations” with a transcript of remarks made by Barbier. In the press release, Barbier again denied the accusations in the Citizen Petition, stating:

“Let me be very clear: I think these allegations are false,” said Remi Barbier, President & CEO. “The allegations claim our science is improbable, unexpected and unique to Cassava Sciences, and therefore it's all an elaborate fraud. By these criteria, all drug innovations are fraudulent. We intend to vigorously defend ourselves and our stakeholders against false and misleading allegations.”

332. In the transcript of his remarks, Barbier further elaborated: “So let me tell you what I think of these allegations, and I won't hold back. These allegations are not only false, I also think they are misleading.” He claimed that “[w]e do not invent stuff out of thin air.”

333. Barbier continued to emphasize and defend Cassava’s longstanding relationship with Dr. Wang, telling investors: “Prof. Wang has also been a scientific collaborator to Cassava Sciences for about 15 years on the Alzheimer’s program. Over 15 years, you get to know someone very well. Based on our long-term scientific relationship with Prof. Wang, we support his scientific integrity and ethics in the strongest possible terms.”

334. Barbier *conceded*, however, that there were “visual errors” in “one publication and one poster presentation” highlighted in the Citizen Petition, but insisted that they “are not material errors” and that, despite the errors, “the data analysis is correct.” First, in the 2017 *Neurobiology of Aging* paper, Barbier admitted that “**Figure 12** contains an image showing 12 control bands. It should show 13.” This issue had specifically been raised by the Citizen Petition. Yet he insisted that “[t]he data analysis was based on all 13 control bands.”

335. Second, Barbier admitted that, as the Citizen Petition noted, the data points in **Figures 4** and **5** of the July 26, 2021 AAIC poster presentation are incorrect. He stated that the spaghetti plot in **Figure 5** of the poster “for the placebo group shows 18 lines; *it should show 20.*” Barbier was quick to claim, however, that “the lines that were visually left out of this spaghetti plot are included in the data analysis.” He added that “[f]igure 5 for the 100 mg group shows 18 lines; *it should show 17.* (The 18th line represents data for an outlier that has been consistently removed from analysis).”

336. But as Dr. Bik noted on Twitter that day in response to Barbier’s comments, “[l]eaving out a value that does not fit with the hypothesis cannot be brushed off as just ‘removing an outlier’ that was left in by error. This is a *very serious and intentional action* that needs much more explanation.” She further Tweeted: “Also, it is hard to imagine a scientist with 3 sets of ~30 data points who accidentally leaves out 2 values in one set and adds an additional value in another set. The data gets plotted from the data (in R). It is not just an artist painting a ‘visual.’”

337. On this news, Cassava’s stock price fell 7.6% to \$50.20 per share, again on unusually heavy trading volume of over 27 million shares.

## IX. DEFENDANTS ATTEMPT TO COVER UP THEIR FRAUD BUT THE TRUTH LEAKS OUT

### A. Defendants Use Doctored Images to Secure November 4, 2021 *Journal of Neuroscience*’s Exculpatory Statement

338. On November 4, 2021, Cassava Science halted its stock trading. Trading halts are temporary suspensions for a particular security at one or more exchanges. They are unusual events, sometimes used in advance of highly significant news about a company.

339. Having captured the attention of the market and news outlets, Cassava issued a press release entitled “Review by Journal of Neuroscience Shows No Evidence of Data Manipulation in Technical Paper Foundational to Cassava Sciences’ Lead Drug Candidate.” In the release, Cassava stated that it had “been informed by the Journal of Neuroscience that there is no evidence of data manipulation in an article it published in July 2012 describing a new approach to treating Alzheimer’s disease.”

340. Seizing on this, Barbier suggested that the Company and its scientists (*i.e.*, Drs. Wang and Burns) had been exonerated. Barbier stated: “I’ve never doubted the integrity of our people or science” and “notwithstanding pundits who may be louder than they are learned. We’ll stay the course until our job is done.” The release further stated: “One human error that does not impact data conclusions was identified (a duplicated panel in Figure 8B of the article), and the publisher is expected to print a correction.”

341. In response to these statements, the Company’s stock price increased by almost 100%.

342. In the press release, Cassava represented that the *Journal of Neuroscience* had “requested raw data for the article, including images of original, uncropped Western blots” and “[h]aving received that data and completed its review, the Journal of Neuroscience states: ‘No evidence of data manipulation was found for Western blot data.’” The release provided the following statement from the journal:

“The Journal of Neuroscience follows COPE [Committee on Publication Ethics] guidelines and takes any claims of misconduct very seriously. In response to allegations of

data manipulation in JNeurosci 2012;32:9773-9784 the Journal requested raw data, including images of original, uncropped Western blots. The Journal determined that there was one duplicated panel in Figure 8 and a Corrigendum was requested and will be printed. No evidence of data manipulation was found for Western blot data.'

343. The statements made above in ¶¶339-342 were false and misleading when made because they failed to disclose that neither Cassava nor Dr. Wang ever provided the “raw data for the article, including images of original, uncropped Western blots,” *but had rather submitted doctored data in an attempt to exonerate themselves.*

344. In fact, on November 10, 2021, when the *Journal of Neuroscience* issued an Erratum to the 2012 publication containing the purported “original” data, Dr. Bik and others raised concerns regarding the integrity of the data within hours of its issuance.

345. The Erratum confirmed that **Figure 8B** contained a duplication, a concern raised by Dr. Bik, noting that “a panel was duplicated in **Figure 8B**. The top left image in the Western blot panel in Figure 8B, representing A $\beta$ 42 immunostaining of FCX of the A $\beta$ 42 group, was duplicated from the top middle image in Figure 8A, representing immunostaining of the FCX of the PTI-125 + A $\beta$ 42 group.”

346. In addition, the Erratum stated: “To provide clarity on the integrity of bands in **Figures 6, A and B, and 9A**, the following images” were “*made available by the authors*” (i.e., Drs. Wang and Burns), who purported to provide the journal with “[t]he original, uncropped blots of loading control bands in **Figure 6, A and B.**” But that was not true.

347. Drs. Bredt and Pitt identified numerous red flags in the Erratum, including:

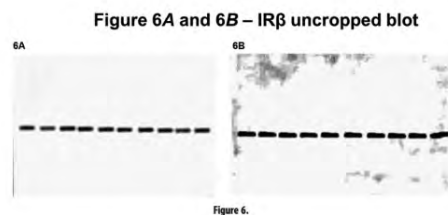
- **First**, the Erratum addresses concerns with images in Figures 6A, 6B, and 9A. The Erratum does *not* address other Figures (e.g., Figures 1, 2, 5, 10, and 11) that have also been noted for apparent data manipulation.
- **Second**, the images supplied as “originals” do not show the edges of the x-ray film from which they were said to have been obtained. Thus, they are *not* the “complete” original images.
- **Third**, the images supplied as “originals” do not show molecular weight markers. Molecular weight markers are standard proteins that are always run in one lane of the gel so that the relative position of the bands-of-interest can be sized. Since no

molecular weight markers were shown, the images supplied as “originals” appear to be, at best, *cropped versions*.

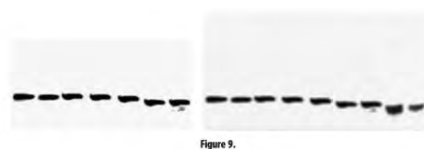
- **Fourth**, the published Erratum reports that for Figure 9A, “[t]he left image is the higher-resolution image with the additional bands cropped out, as seen in the full image on the right.” The supplied “original” images are of lower resolution than the images published in the 2012 paper. Resolution of the original should be *higher*, not lower, than subsequent ones.

348. Independent forensic analysts also found evidence that the purportedly “original” images were in fact *composites of cropped images, and thus not originals at all*. Within hours of the Erratum being published, Dr. Bik, in particular, began Tweeting her concerns and posting them on PubPeer. She wrote, regarding the purported “original,” uncropped blot scans for **Figures 6A/6B and 9A** (below), “[b]ut these appear to show just the cropped blots on a larger area, with none of the expected MW marker positions, labels, or edges of the X ray film visible.”

2 • The Journal of Neuroscience, 0, 2021 • 00000:1–2



**Figure 9A –  $\beta$ -Actin uncropped blot**

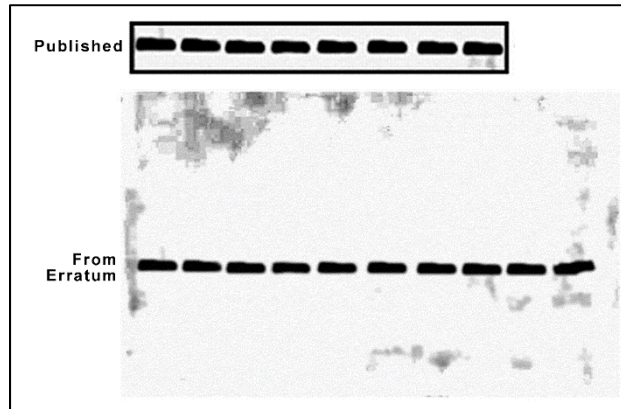


DOI: 10.1523/JNEUROSCI.2154-21.2021

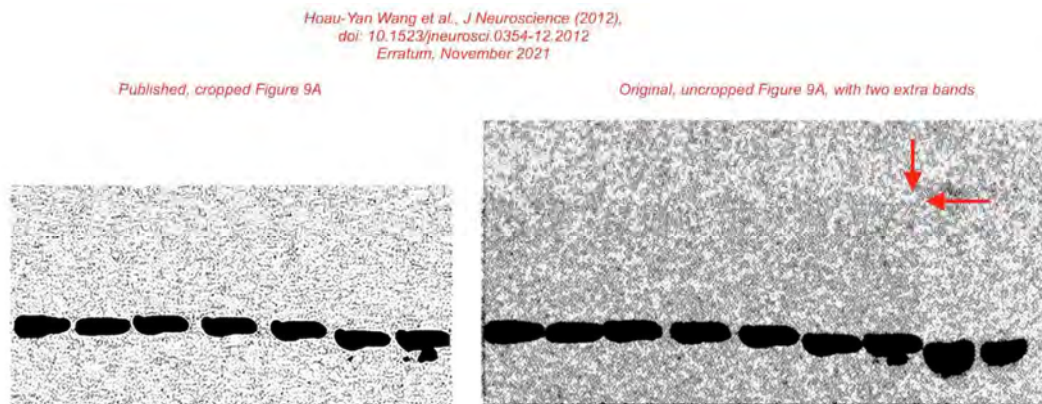
349. On this news, Cassava’s stock price dropped 11.5%, or \$9.01 per share, closing at \$69.40 per share on November 10, 2021.

350. Dr. Rossner similarly found that the overall pixelation patterns in the backgrounds of the first published and Erratum images of **Figure 6B** (below) differ from one another. The background in the published image is in a grid pattern, whereas the background in the supporting image from the Erratum is

speckled. As a result, this difference provides additional evidence that the images in the Erratum *are not authentic source data for the published images*.



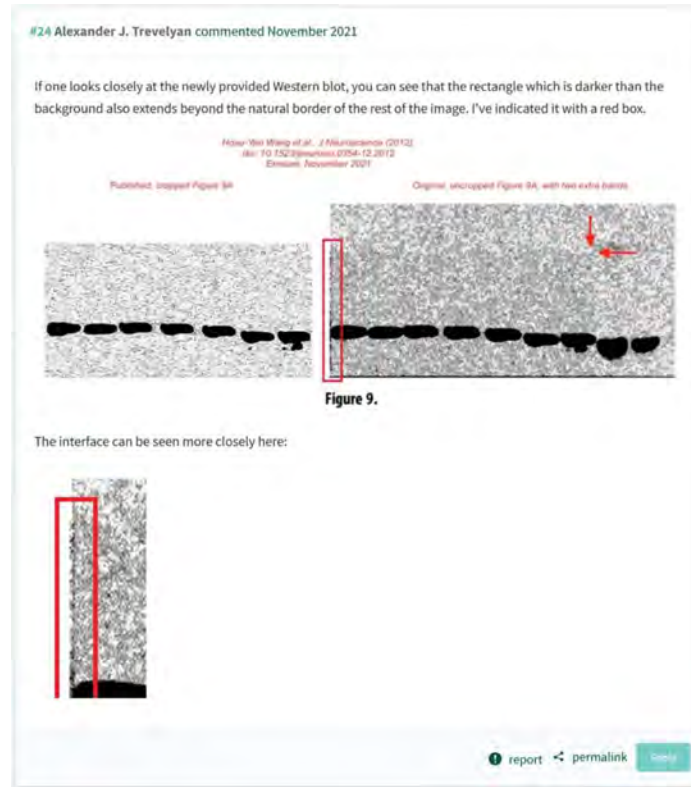
351. For **Figure 9A**, Dr. Bik adjusted the contrast on the “original” image, revealing an alteration in the background (*see below*). She stated: “There is a potential ***big concern*** in the provided original  $\beta$ -actin blot for **Figure 9A**. The authors/journal say the blot on the right shows the original blot with two additional lanes on the right. But I see a box around those lanes that matches the published blot’s size.”



**Figure 9.**

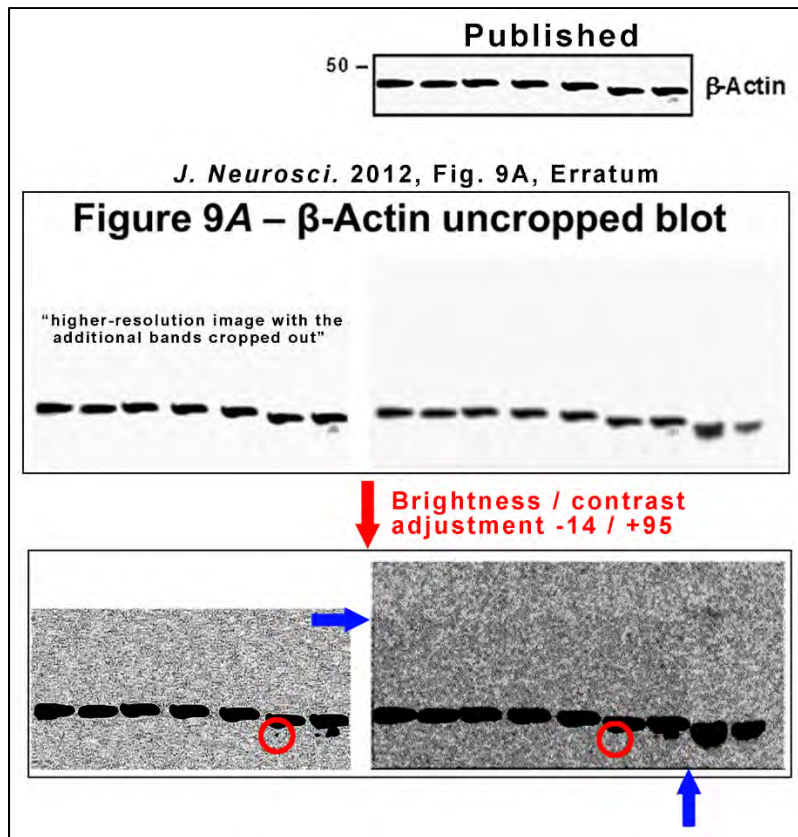
352. Alexander Trevelyan, Ph.D., supplemented Dr. Bik’s analysis on PubPeer showing an unexpected partial “edge” on the left side of the figure, as well:





353. Dr. Rossner found, too, that the brightness/contrast adjustment revealed linear inconsistencies in the background of the right-hand image for **Figure 9** from the Erratum (see blue arrows at the bottom right of the illustration below). Dr. Rossner concluded that such inconsistencies *can indicate that an image has been spliced* (either a region has been spliced out, juxtaposing regions of non-matching background, or a region has been spliced in with a non-matching background).





354. In sum, as the November 17, 2021 supplement to the Citizen Petition concluded: “The bottom line is Cassava Sciences **does not** appear to have provided the Journal of Neuroscience ‘original, uncropped Western blot’ as represented in its 11/4/2021 press release, so the journal could not have exonerated them, as they so dramatically suggested.” The petition supplement continued, “[m]aking matters far worse, the company appears to have **knowingly** taken the published image (the one of the left above), blurred it a bit, and then photoshopped it onto a slightly different canvas to ‘create’ the image on the right.” In fact, ***all of the images provided in the addenda are cropped images and not full scans. Thus, they do not constitute the original source data.***

355. Communications obtained pursuant to FOIL requests validate these concerns. On November 3, 2021, ***the day before*** Cassava’s November 4 press release, emails between the editor-in-chief of the *Journal of Neuroscience*, Marina Picciotto, and Dr. Wang reflect that, according to Dr. Wang, it was purportedly “more difficult than I anticipated to find the blots” and that Dr. Wang merely provided a

“powerpoint containing the requested uncropped blots” **not** the original, “raw data.” Accordingly, the *Journal of Neuroscience* could not have authenticated Dr. Wang’s images without access to the originals. Indeed, pursuant to principals outlined by the Office of Research Integrity for the U.S. Department of Health and Human Services, “[a]uthentication of a scientific image **requires** access to the original data.” And importantly, “in the case where an image lacks authenticity, the **absence of the original data can be used as evidence of possible research misconduct** and sufficient justification to conduct further fact finding.”

356. Email communications obtained pursuant to FOIL also confirm Cassava’s and Dr. Burns’s involvement in this scheme. On September 30, 2021, Dr. Burns emailed Dr. Juan Lerma Gomez, the editor-in-chief of a different journal, *Neuroscience*, in an attempt to clear Defendants of allegations of data manipulation in their 2005 paper in that journal. Dr. Burns wrote in her email to Dr. Gomez “**we** have already responded to JNS [Journal of Neuroscience] with **original blots** (exonerating claims of fraud). . . .” But, as detailed above, Dr. Burns never provided “original” data to the *Journal of Neuroscience*.

357. Tellingly, after Dr. Bik raised her concerns regarding the authenticity of the purported “original” data Drs. Burns and Wang supplied, the journal **changed** their Editorial Note into an Expression of Concern on December 17, 2021. It acknowledged the issues and deferred further judgment until CUNY finished its still ongoing investigation:

The editors have been made aware of concerns about Western blots in this study **including** those published with the article’s erratum (Wang et al., 2021). These and other concerns are currently under investigation by the academic authorities at the [CUNY]. JNeurosci will await the outcome of that investigation before taking further action.

358. That same day, the journal also issued **another** Expression of Concern for Dr. Wang’s 2008 paper “Dissociating  $\beta$ -Amyloid from  $\alpha 7$  Nicotinic Acetylcholine Receptor by a Novel Therapeutic Agent, S 24795, Normalizes  $\alpha 7$  Nicotinic Acetylcholine and NMDA Receptor Function in Alzheimer’s Disease Brain”:

JNeurosci is publishing an Expression of Concern for the article, “Dissociating  $\beta$ -Amyloid from  $\alpha 7$  Nicotinic Acetylcholine Receptor by a Novel Therapeutic Agent, S 24795, Normalizes  $\alpha 7$  Nicotinic Acetylcholine and NMDA Receptor Function in Alzheimer’s Disease Brain,” by Hoau-Yan Wang, Andres Stucky, JingJing Liu, Changpeng Shen, Caryn Trocme-Thibierge, and Philippe Morain, which appeared on pages 10961-10973 of the September 2, 2009 issue. The editors have been made aware of concerns about Western blots in this study. These and other concerns are currently under investigation by the academic authorities at the [CUNY]. JNeurosci will await the outcome of that investigation before taking further action.

359. News of the Expressions of Concern spread on Twitter. During the afternoon of December 17, 2022, Dr. Bik Tweeted: “After first issuing a correction using blots that raised even more concerns, the journal is now doing the right thing: issuing an Expression of Concern while awaiting the results of an institutional investigation.”

360. On this news, Cassava’s stock price fell 15.6%, or \$6.82 per share, between Friday, December 17 and Monday December 20, 2020, to close at \$36.77 per share.

361. Dr. Bik later noted on Twitter regarding the journal’s course correction in issuing the Expressions of Concern that “[s]ome Editors of Scientific journals are naïve when it comes to image concerns – what authors provide as original materials might not always be what they claim.” In his later review of these materials, Dr. Rossner similarly concluded that *the editors who accepted these images as “source data” did not apply the standard of data integrity expected of journal editors when they are evaluating allegations of image manipulation or duplication.*

362. Dr. Bik has also explained that publishers may hesitate to retract bad articles, since every cited paper increases a journal’s citation ranking. (In recent years, some researchers have also sued journals over retractions.) She is appalled at how editors routinely accept weak excuses for image manipulation – it’s like “the dog ate my homework,” she said.

**B. Cassava’s November 15, 2021 Form 10-Q**

363. On November 15, 2021, Cassava disclosed in its Form 10-Q for Q3 2021 filed with the SEC that “[c]ertain government agencies have asked us to provide them with corporate information and documents.”

364. On this news, Cassava’s stock fell another 12%, or \$8.29 per share, to close at \$60.51 per share, on November 15, 2021.

365. The Form 10-Q misleadingly failed to disclose, however, that multiple government agencies, including the DOJ, SEC and NIH, had opened investigations *into Cassava* and that the DOJ probe, in particular, was a *criminal* investigation.

366. Barbier later confirmed in a July 27, 2022 statement that Cassava knew of these investigations into the Company, including the criminal DOJ probe, at the time of the November 15, 2021 Form 10-Q disclosure. In response to the news of the DOJ investigation, the Company issued a July 27, 2022 press release that stated “[i]n November 2021, Cassava Sciences *previously disclosed* that certain government agencies had asked for corporate information and at that time, the media widely reported on these prior disclosures.”

**C. A November 17, 2021 Wall Street Journal Article Reveals Investigations into Cassava and Dr. Wang**

367. Then, two days later, on November 17, 2021, *The Wall Street Journal* published a story on Cassava revealing that “The [SEC] is investigating claims that [Cassava], SAVA – 23.45% the sixth-best performing U.S. stock this year, manipulated research results of its experimental Alzheimer’s drug, according to people familiar with the matter,” and that the investigation followed an August 2021 meeting between the SEC and Drs. Bredt and Pitt. The article also revealed that, according to Barbier, the NIH, which awarded \$20 million in grants to Cassava and its academic collaborators since 2015 for drug development, was also examining the claims. Barbier further confirmed that CUNY had begun an inquiry.

368. In fact, pursuant to documents obtained via a FOIL request, by November 9, 2021, CUNY's inquiry report (which has not been made public) had been submitted to Dr. Wang and his attorney, and they were informed that CUNY's president, Dr. Vincent Boudreau, had decided to refer the case to CUNY for a full investigation of the misconduct.

369. *The Wall Street Journal* article also revealed the identities of Drs. Bredt and Pitt, whom the newspaper interviewed for the article, as the Citizen Petition's authors. In the article, Barbier continued to deny the doctors' claims, stating (and changing his story multiple times within the space of a single sentence): "There is zero evidence, zero credible evidence, zero proof that I've ever engaged in, nor anyone I know, has ever engaged in funny business." Barbier further replied in an email to reporters that the allegations lodged against his Company were "outlandish."

370. As reported in *The Wall Street Journal*, however, "[s]everal other scientists interviewed by *The Wall Street Journal* said some images in the articles depicting experimental results appear to have been copied and pasted from other sources," including Drs. Bik and Rossner. In the article, Dr. Bik confirmed that she "concurred with many of the claims in the petition" and said that she "found other potentially manipulated images in papers describing how Simufilam works." Dr. Rossner, whom Plaintiffs later retained in this matter, told the newspaper that "many of the accusations merited further investigation."

371. Barbier, however, dismissed their concerns, stating: "In order to make allegations on the scale that they have, in order for those allegations to be credible, *you've got to look at the originals*," he said. "Blowing up western blots and, you know, looking for funny faces or funny shapes or whatever . . . it doesn't have legitimacy." Yet, Barbier has never publicly released the originals or the results of any independent review of the originals.

#### **D. The November 17, 2021 Citizen Petition Supplement**

372. In their November 17, 2021 third supplement to the Citizen Petition, Drs. Bredt and Pitt revealed that "at least three of the nine biomarkers analyzed by Dr. Wang and published by Cassava for the

phase 2a study of simufilam in Alzheimer's disease also appear to have wildly anomalous baseline measures," similar to the biomarkers analyzed by Dr. Wang and presented by Cassava in the phase 2b study of simufilam in Alzheimer's disease with "baseline values so far outside expectations that they suggest lab errors or manipulation."

373. The November 17, 2021 third supplement also highlighted that certain of Cassava's experiments were "seemingly undoable." The supplement explained:

[T]he alpha7 version of the nicotinic acetylcholine receptor (nAChR) is central to simufilam's proposed mechanism in Alzheimer's disease. In their 2017 review (Neuroimmunology and Neuroinflammation 4: 263), Drs. Burns and Wang state that "PTI-125 binds and reverses the altered FLNA conformation to prevent A $\beta$ 's signaling via  $\alpha$ 7nAChR and aberrant activation of TLR4, thus reducing multiple AD-related neuropathologies." Like most of their claims, this research is unique to Drs. Wang/Burns/Cassava and relies heavily on Western blotting. These results are elaborated in Cassava's 2012 Journal of Neuroscience paper and their 2017 Neurobiology of Aging paper.

***A major problem with this is that international leaders in the nAChR field agree that there are no antibodies suitable for Western blotting of alpha7 nAChR in the brain*** (see: Moser et al. Evaluating the suitability of nicotinic acetylcholine receptor antibodies for standard immunodetection procedures Journal of Neurochemistry, 2007, 102, 479–492). Therefore, the alpha7 nAChR data that form a mechanistic foundation for simufilam ***seem scientifically undoable***.

374. As a result, "[t]his fundamental limitation for alpha7 nAChR Western blotting raises serious questions regarding the validity of **Fig. 1A, Fig. 2A, Fig. 9A, Fig. 10A, and Fig. 12A** in Cassava's 2012 *Journal of Neuroscience* paper," which had been previously criticized in the Citizen Petition.

375. These concerns had first been flagged by Dr. Adrian Heilbut on Twitter on November 9, 2021, after markets had closed. He noted that, for the 2012 *Journal of Neuroscience* and 2017 *Neurobiology of Aging* papers, Drs. Wang and Burns used an antibody specific for the alpha1 subunit of the nAChR, yet reported that they were able to detect the alpha7 nAChR in brain tissue. As the November 17, 2021 supplement explained:

Western blots rely on antibodies that recognize specific proteins. Thus, an antibody to the alpha1 nAChR does not recognize the alpha7 nAChR. The alpha1 nAChR is primarily found in muscle tissue and ***not in the brain***. Using an alpha1 nAChR antibody to detect

alpha7 nAChR in brain is *senseless*. It would be like checking for Covid-19 infection with a pregnancy test kit.

376. For the 2012 *Journal of Neuroscience* paper, Drs. Wang and Burns claim to use two antibodies from Santa Cruz Biotechnology. One is catalog # SC-5544, which according to the supplement,

***does not work for Western blotting at all.*** This limitation is stated explicitly in a 2017 paper (J Histochem Cytochem. 65: 499-512), which states ‘Figure 2 shows four antibodies that fail to recognize rat  $\alpha 7$  nAChRs on western blots: Santa Cruz sc-5544 (H-302) . . .’ Undeterred, their 2012 *Journal of Neuroscience* paper shows several Western blots claiming to detect alpha7 nAChR by Western blotting.

377. “Even worse,” said the supplement, “Drs. Wang and Burns also mention antibody catalog # SC-65844 in their 2012 *Journal of Neuroscience* paper. However, Santa Cruz Biotechnology sells this to detect the alpha1 nAChR, ***not the alpha7 nAChR***. For the *Neurobiology of Aging*, they only mention using SC-65844, which detects alpha1 and ***not*** alpha7 nAChR.”

378. The November 17, 2021 third supplement concluded, “[i]n the end, all their purported alpha7 nAChR Western blotting research in the brain is seemingly undoable. Furthermore, they didn’t even use an alpha7 nAChR antibody in one of their most important foundational studies.”

379. As a result of these revelations, Cassava’s stock price declined 23.7%, or \$14.62 per share, to \$47.07 per share, on November 17, 2021.

#### **E. The December 8, 2021 Citizen Petition Supplement**

380. In their fourth supplement to the Citizen Petition, dated December 8 2021, Drs. Bredt and Pitt wrote that they had found “irrefutable evidence of data manipulation/fabrication” in a crucial experiment in Cassava’s 2017 *Neurobiology of Aging* paper, previously criticized in the Citizen Petition, demonstrating simufilam’s purported method of action for treating Alzheimer’s disease – binding to filamin A. Specifically, Drs. Bredt and Pitt wrote that

recent re-inspection of the Methods section for this crucial experiment shows seemingly ***irrefutable evidence*** of data manipulation/fabrication. The section states: “PTI-125’s affinity for FLNA was determined in immunopurified FLNA using [C14]PTI-125 (57.7 Ci/mmol) . . . . Briefly, a binding curve was generated by incubation of 0.1  $\mu$ g immunopurified FLNA from control or AD hippocampus . . .” Importantly, the binding



experiments used PTI-125 labeled with carbon-14 [C14], which has a relatively low specific activity (rate of decay). This physical law makes [C14] useful for carbon dating, but ***completely unsuitable for detecting high affinity binding like that claimed for PTI-125 and filamin A.***

A few of the many major problems identified in the supplement are:

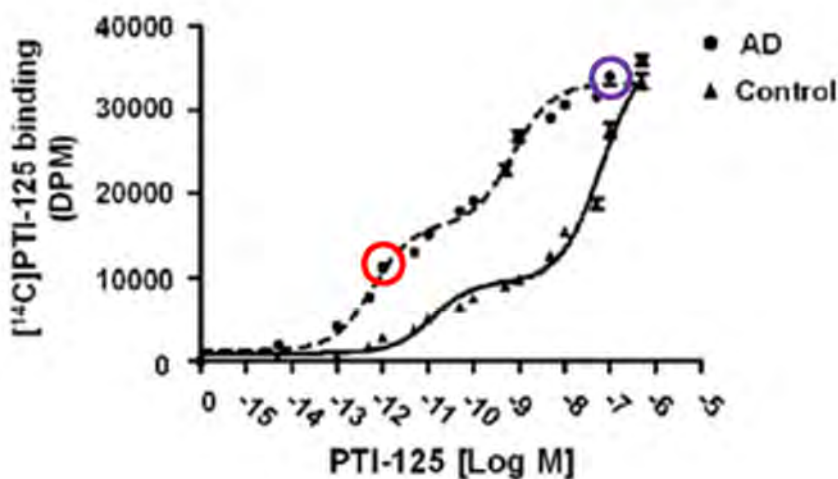
381. ***First, The Claimed Specific Activity for [C14] PTI-125 is ~1000 Greater Than***

**Physical Laws Allow:**

Cassava states that their [C14] PTI-125 has a specific activity 57.7 Ci/mmol. However, pure [C14] has a specific activity of 62.5 mCi/mmol = 0.0625 Ci/mmol. This is the upper limit for a molecule with one [C14] substitution. Assuming one [C14] as is likely, Cassava's claimed specific activity for PTI-125 is ***~1000 times higher than theoretically possible.*** Such an inexplicable error would create insurmountable problems and ***invalidate the study.***

382. ***Second, FLNA Binding [C14] PTI-125 Could Maximally Yield 47 DPM vs >30,000***

**DPM Claimed in Fig. 1B:** "Because [C14] has intrinsically low specific activity (0.0625 Ci/mmol), it does not yield sufficient "counts" (DPM, disintegrations per minute) to reliably detect receptor binding." Drs. Bredt and Pitt calculated the maximum number of DPM that could be achieved based on Cassava's methods, arriving at a 47 DPM maximum, which dramatically clashes with ~30,000 DPM claimed by Cassava scientists in **Figure 1B** (below, see purple circle).



383. **Third, [C14] PTI-125 Cannot be Used to Detect 1 pM FLNA Binding Affinity:** In the red circle of **Fig. 1B** (above), Cassava claims 10,000 DPM binding at 1 pM ( $1 \times 10^{-12}$  M) PTI-125. But, according to the supplement, “[b]asic radiochemistry illustrates why this is *impossible*,” because “for Cassava to detect 10,000 DPM (red circle in **Fig 1B**), they would require  $10,000 \text{ DPM} \div 137 \text{ DPM/liter} = 73 \text{ liters}$ .” Cassava’s binding assays, however, “surely were performed in much smaller volumes, and likely used  $<5 \text{ mL}$ , if the experiments were done at all.”

384. These numerous additional elementary problems with Cassava’s experiments further undercuts *whether Simufilem binds to Filamin A at all*. The supplement concluded: “Fatal flaws in these critical binding experiments, which form the foundation for their key investigations, raise serious questions about Cassava’s hypotheses that filamin A is relevant to Alzheimer’s disease and about whether simufilem affects filamin A.”

385. On this news, Cassava’s stock price closed at \$45.86 per share, an 8.2% decline of \$4.12 per share from the prior day’s closing price.

#### **F. Defendants Use Doctored Images to Secure *Neuroscience*’s December 20, 2021 Exculpatory Statement**

386. On December 21, 2021, Cassava issued a press release “Science Journal Finds No Evidence to Support Claims of Data Manipulation in 2005 Publication.” The release quoted Barbier:

“*Another science journal [Neuroscience] has cleared us of allegations . . . . This clearance is from an independent third party who is neutral and expert in the field. This reinforces my conviction that false and misleading allegations of scientific misconduct being made against us are simply designed to enrich those making them.*”

387. The release also included the following excerpt of a December 20, 2021 Editorial Note from the journal:

“In response to allegations of data manipulation in an article published in *Neuroscience* Vol 135, Issue 1, 2005, Pages 247-261, and following COPE (Committee on Publication Ethics) guidelines, *the journal asked the authors for images of the original, uncropped Western blots from this study. After careful examination of these original material, Neuroscience found no evidence of manipulation of the Western blot data or other figures of this publication.*”

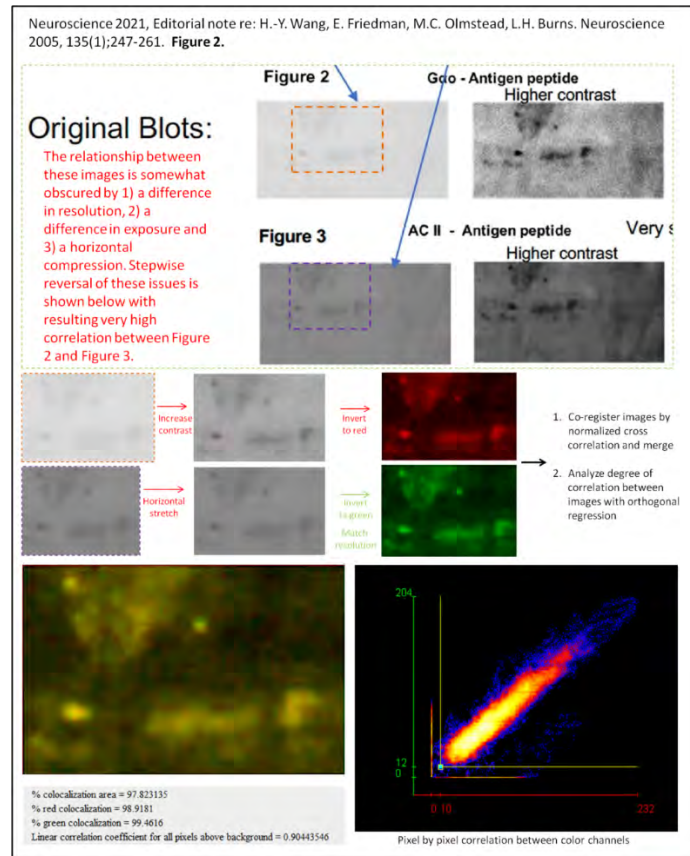
388. The complete version of the journal’s statement, however, included the following line *not* included in Cassava’s press release, that the journal was reserving and deferring further judgment until after the CUNY investigation: “If any subsequent information arises from an institutional investigation, this will be considered once available.”

389. Moreover, the authors, Drs. Wang and Burns, did *not* provide the original, uncropped Western blots to the journal, as they represented to *Neuroscience* and as Cassava represented to the public in the Company’s December 21, 2021 press release. For this reason, the statements in ¶¶386-387 were false and misleading when made.

390. After reviewing the blots in **Figures 2, 3, and 5**, which the journal made publicly available with their statement, Dr. Bik Tweeted on December 20: “But as with the J Neuroscience correction, I am not sure if these are indeed original.” Bik highlighted that “[t]he provided uncropped blots *should actually be X-ray films*, as stated in the paper. *Instead*, the authors provided images without blot edges, labels, or markers.” Dr. Bik further stated that for two blots in **Figures 2 and 3**: “I would argue these show the *exact same blot*, albeit at different resolution. Was the editor fooled here?” And “even more concerning,” Dr. Bik found “the provided ‘originals’ for **Figure 5** all show very similar backgrounds. They look like the published blots projected on the same background, *perhaps similar to what happened with the J Neuroscience paper*.”

391. Dr. Bik wrote in further detail on PubPeer that, for the concern regarding **Figures 2 and 3**, “these original blots actually look very similar. They are presented at different resolution/compression and crop, *but they do not take away my concern* that the top Gao panel in **Figure 2** is very similar to the ACII panel in **Figure 3**.” In addition, her “concern about the rectangular area around the band in the top Gao panel in Figure 2 does *not* appear to have been addressed.”

392. Another PubPeer commenter agreed with Dr. Bik’s concerns and provided their analysis regarding **Figures 2 and 3**:

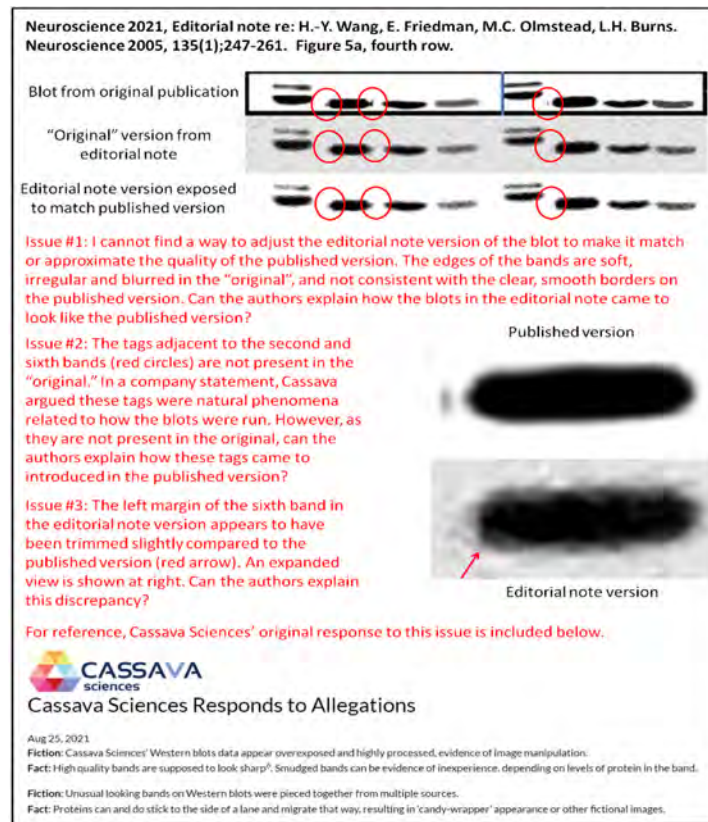


393. Regarding **Figure 5**, Dr. Bik also provided additional detail on her findings on PubPeer, stating:

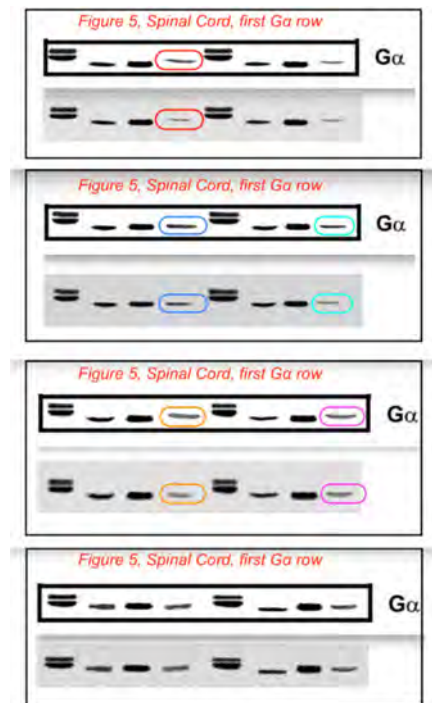
*None of these blots look like the expected uncropped X-ray films*; there are no marker lanes or labels, or edges of the blot visible. Yet, the article state the blots were exposed to X-ray films. How could the authors then provide scans of blots.

*Even more concerning*, the blots provided in this Editorial Note appear to show very similar background patterns, albeit shown at different resolutions. *How can the authors explain that?*

394. Dr. Bik further agreed with the additional concerns raised on PubPeer regarding **Figure 5A** stated below:



395. And Dr. Bik raised new concerns about **Figure 5B**, as well, noting further “discrepancies between the published blot of **Figure 5[B]** and the originals provided in the Editorial Note of December 2021.” Dr. Bik wrote that: “Comparing the published Gα rows to the provided original [see below], the bands in the fourth and eight lanes in particular do not always seem to match each other. I have highlighted those here with rounded boxes of the same color.”



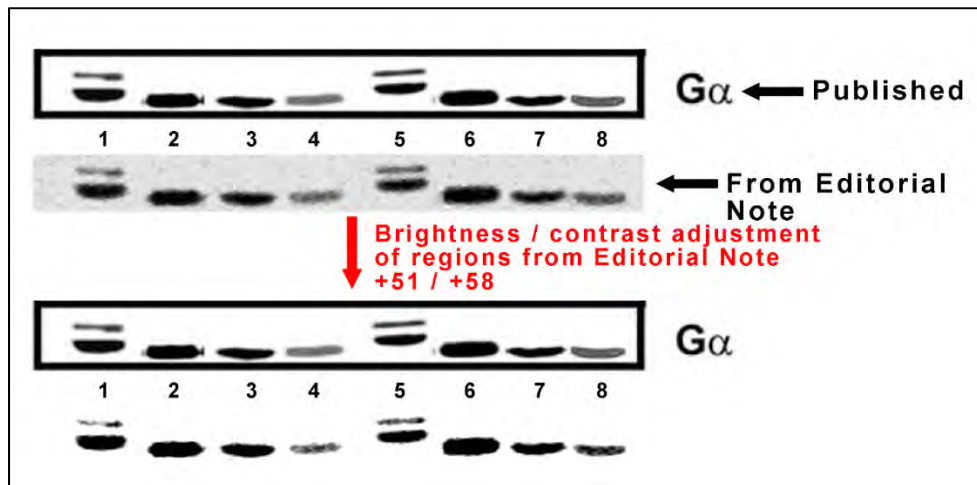
396. Dr. Rossner, too, disagreed with the journal’s opinion that it “found no evidence of manipulation of the Western blot data or other figures of this publication.” Rather, the authors had not dispelled the concerns raised in the allegations related to the data in this journal, as *all of the images provided in the December 20, 2021 Editorial Note are cropped images and not full scans. Thus, they do not constitute the original source data, as claimed in the Editorial Note.*

397. Regarding the supporting image provided in the Editorial Note for **Figure 5A**, Dr. Rossner also found that the bands were missing the sharp edges and band remnants that are present on the sides of the bands in the published article. *It thus appears that the authors removed these aspects digitally when preparing the image for the Editorial Note and that elements that were present in the published image were deleted in the image submitted for the Editorial Note, perhaps to hide the manipulation that was apparent in the published image.*





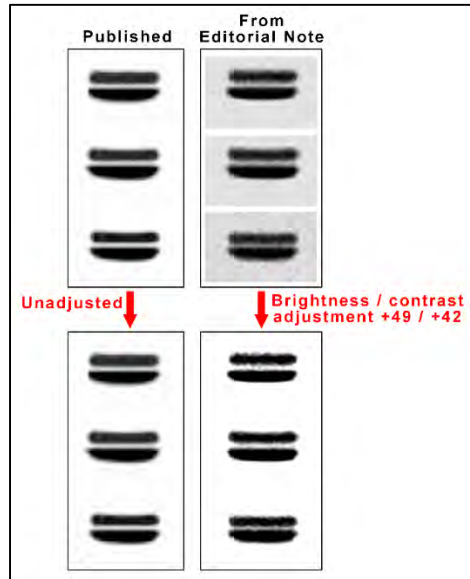
398. In addition, based on the different band shapes, sizes and intensities, the bands in lanes 4 and 8 (below) do not appear to match between the published image and the image in the Editorial Note. Thus, in one of those images, *the bands in those lanes appear to have been replaced with other bands, or they might have been altered using image-processing software.*



399. Accordingly, Dr. Rossner found that the supporting data provided in the Editorial Note *do not dispel the concerns about splicing in the published image* in Figure 5A.

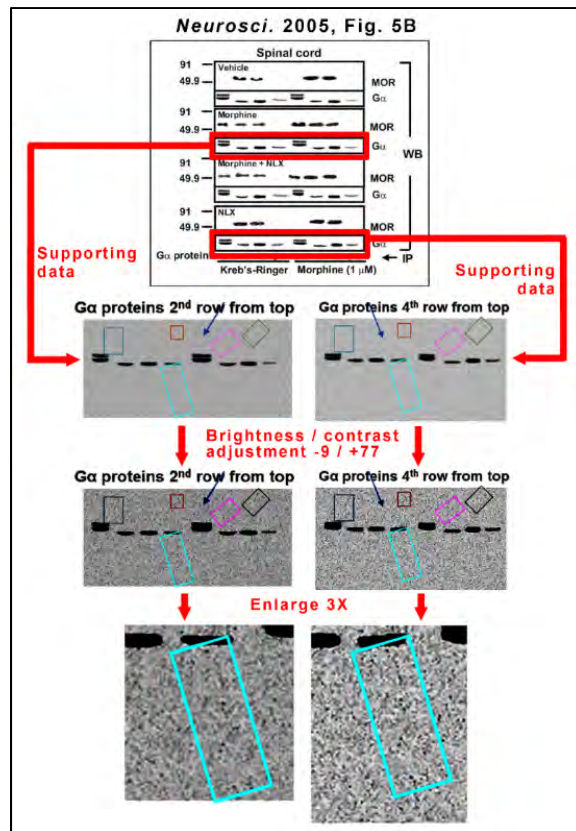


400. In **Figure 5B**, Dr. Rossner found in a comparison of the published lanes and the lanes provided in the Editorial Note appended to the article, that the top and bottom sets (*see below*) do not appear to match the published bands.



401. Dr. Rossner further agreed with the new concerns Dr. Bik described in ¶395 regarding **Figure 5B** and concluded that these differences further call into question the authenticity of the images supplied as “source data” in the Editorial Note.

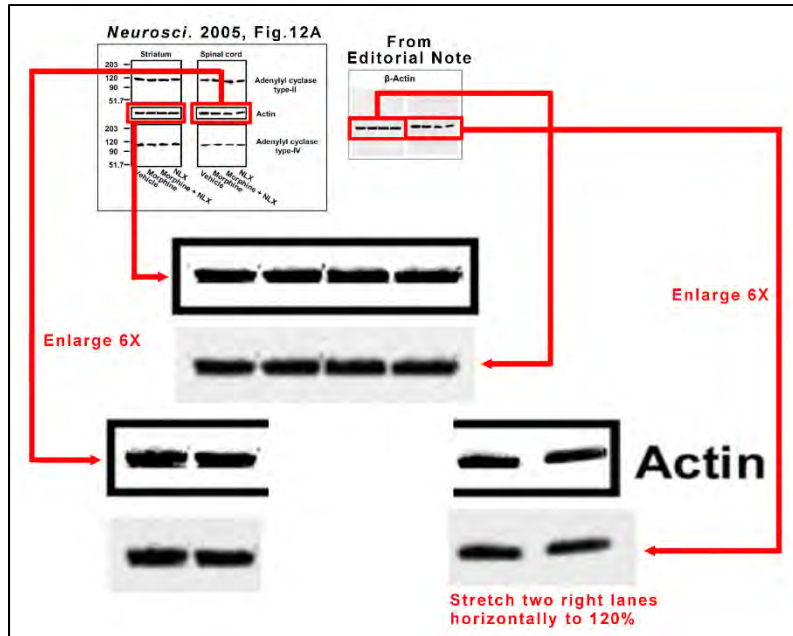
402. Finally, Dr. Rossner concurred with the concerns raised by Dr. Bik of duplication of the background in two of the images provided as supporting data for **Figure 5B** in the Editorial Note. Regions of background in the two images that appear to be duplicated are highlighted (below) in the rectangles of matching color.



403. *It is not possible for this similarity to occur naturally.* Thus, Dr. Rossner concluded that it appears that individual bands (or band doublets) may have been copied and pasted onto a falsified background to fabricate these images.

404. Last, Dr. Rossner compared the published Actin panels from **Figure 12A** to the images provided in the Editorial Note. He concluded that the images taken from the Editorial Note were *not originals* but rather additional duplicates.

405. Based on similar band shapes, sizes, intensities, edge elements, background elements, and relative positions, Dr. Rossner is highly confident that the images provided in the Editorial Note match the published images (below). Thus, in both the published set of images and the set of images provided in the Editorial Note, the vertically aligned bands are duplicates derived from the same source image. That is, the supporting image data provided by the authors in the Editorial Note contain *duplicated bands*, and they *do not dispel the concerns raised by the Citizen Petition*.



406. Documents obtained pursuant to a FOIL request further support that the original source data for these figures was never provided to *Neuroscience* and was possibly destroyed. On November 16, 2021, Dr. Burns emailed Dr. Juan Lerma Gomez, the editor-in-chief of *Neuroscience*: “We are still looking for the original blots in backup drives, since the original hard drive melted years ago.” This email also confirms that Dr. Burns and Cassava were involved in providing the so-called “original” images to the journal.

407. Furthermore, as of November 15, 2021, Dr. Gomez advised Drs. Burns and Wang that the journal intended on publishing an Expression of Concern regarding the 2005 paper until the CUNY investigation concluded. For reasons unknown, however, following communications between Dr. Gomez and Dr. Burns, *Neuroscience* did not publish that Expression of Concern.

#### **G. Dr. Wang Attempts to Use Doctored Images in *Molecular Neurodegeneration* to Prevent January 3, 2022 Retraction**

408. In September 2021, numerous commentators on PubPeer, including Dr. Bik, raised concerns regarding Western blots in **Figure 9** of the 2021 paper in *Molecular Neurodegeneration*, “Calcium-dependent cytosolic phospholipase A activation is implicated in neuroinflammation and

oxidative stress associated with ApoE4,” which, notably, Dr. Wang’s lab had produced. On January 3, 2022, the paper’s corresponding author, Dr. Hussein N. Yassine, responded on PubPeer, stating:

We have been notified of these irregularities in Figure 9. *We do not have a clear explanation for them.* We have consulted with the publisher and journal. *All authors agreed to retract the paper* and resubmit without figure 9. Ongoing experiments are conducted to replicate experiments in Figure 9 to ensure the rigor and validity of the findings.

409. On January 20, 2022, Alex Trevelyan, Ph.D., posted on Twitter that he “received confirmation from Molecular Neurodegeneration that *HY Wang did indeed attempt to provide apparently manipulated images to the journal*, but that they did not accept them. Original blots were requested but *Dr. Wang could not provide them.*” In a message from the journal to Dr. Trevelyan, the journal stated:

When the potential integrity issues was called to our attention, Dr. Yassine requested the original blot images from Dr. HY Wang for MN’s editorial team and Springer Nature’s Research Integrity Group to examine. *Unfortunately, these “original” blot images from Dr. HY Wang also had visible signs very much looking like image manipulation, and Dr. Wang said he couldn’t find other images from the repeated experiments.*

410. The message further stated: “After reviewing the ‘original’ blot images provided by Dr. HY Wang, all the authors, editors, and our publisher agreed retraction is the right call in this case.”

#### **H. The FDA’s February 10, 2022 Response to the Citizen Petition**

411. On February 10, 2022, the FDA issued a response to the Citizen Petition. In the response, Dr. Patrizia Cavazzoni, Director of the FDA’s Center for Drug Evaluation and Research, “acknowledge[d] the importance of the issues” the Citizen Petition raised and further stated that the FDA “take[s] the issues you raise[d] seriously.” The FDA, however, denied the petition on technical grounds, finding that the Citizen Petition’s request for the FDA to initiate an investigation was not an appropriate request under the citizen petition process. Indeed, the FDA’s response took special care to note “that your Petitions are being denied *solely* on the grounds that your requests are not the appropriate subject of a citizen petition,” and that “[t]his response does not represent a decision by the Agency to take or refrain from taking any action relating to the subject matter of your Petitions.”

412. Yet when Cassava issued a press release on February 10, 2022 regarding the FDA’s letter, it disingenuously suggested that Cassava had been cleared of wrongdoing by the FDA. The release quoted Barbier as stating: “‘The news is very welcome but not surprising . . . . We said from the outset that the allegations are false. I think the message may be that the FDA’s citizen petition privilege is not to be trifled with by stock market participants.’”

413. Moreover, Barbier has continued to knowingly spread false information regarding the FDA’s response to the Citizen Petition. According to an analyst at Univest Securities, during an April 27, 2022 question and answer session during the B. Riley Securities Conference, “Mr. Barbier responded to a question regarding the Citizen’s Petition and stated that the FDA denied the petition *because they did not find any evidence of fraud.*” As the analyst pointed out, however,

[w]hile the FDA did deny the Citizen’s Petition, it was *not* because the FDA did not find evidence of fraud based on the evidence presented. According to the response letter from the FDA, “it was denied solely on the grounds that your requests are not the appropriate subject of a citizen petition.” The FDA also stated that further action related to the subject has not been decided at that time.

#### **I. The March 22, 2022 Expression of Concern in *Neurobiology of Aging***

414. On March 22, 2022, the journal *Neurobiology of Aging* issued an Expression of Concern for Drs. Wang’s and Burns’s 2017 paper “PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer’s disease pathogenesis.”

415. The Expression of Concern stated:

A reader has made the editors aware of concerns regarding the above-referenced report published at *Neurobiology of Aging*. These issues were conveyed to the authors, who provided a detailed response, including images of relevant uncropped western blots and photomicrographs, as the editor requested. The material was evaluated by an independent expert with relevant methodological expertise, the manuscript was scanned by AI-based figure proofing software (i.e., Proofig), and all available input was considered by the handling editor and Editor-in-Chief.

416. The Expression of Concern further stated that while the editors did not find “compelling evidence” of data manipulation “intended to misrepresent the results,” the journal did find an extensive list of errors in the paper, many of which had been identified by the Citizen Petition:

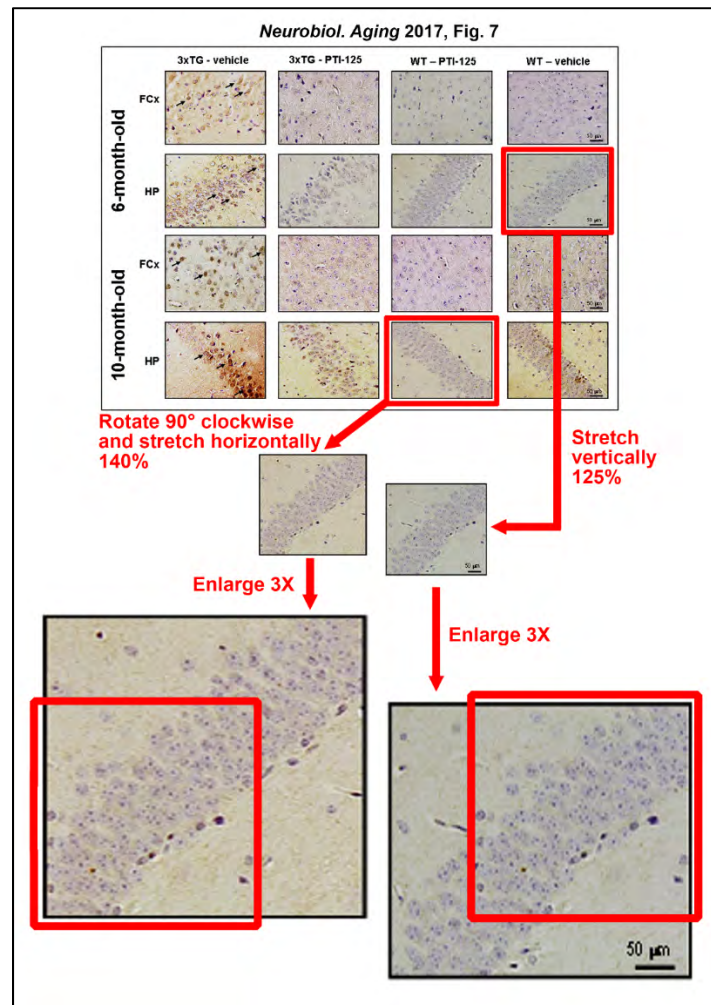
- The commercial catalog number listed for the primary anti-body against  $\alpha 7$  nicotinic receptor is incorrect.
- The specific activity of the C14 -PTI-125 is incorrect.
- The filamin A (FLNA) concentration in the binding assay is incorrect.
- The scintillation counter used to assay C14 was not properly calibrated or configured for the C14 radioisotope, and the absolute values reported are not reliable.
- In Figure 7, the 10-month-old HP panel for the WT - PTI-125 group is duplicated as the 6-month-old HP panel for the WT - vehicle group.
- Labeling in the key to Figure 12, lane 8, is incorrect.
- NR1 loading controls in Figure 12 were not measured from stripped re-probed gels as indicated in the published report; they were run on separate gels and one lane was omitted in Figure 12.
- Whereas the composition of Figure 12 suggests that all conditions were run on the same gel, conditions were in fact split across two gels (without internal controls or repeats).

417. Moreover, the Expression of Concern deferred judgment until after the CUNY investigation is complete and reserved further corrective action, concluding: “Neurobiology of Aging is aware of an ongoing inquiry of these and other concerns by the sponsoring institution, the [CUNY], and *will make a final decision as to appropriate corrective action once that inquiry has been concluded.*” Unlike other journals, however, the Expression of Concern did not provide the purported “uncropped Western blots” for analysis of whether original data had actually been provided to the journal.

418. There is, however, evidence of *deliberate* data manipulation in this paper. For example, the journal acknowledged the duplication in **Figure 7**, but the changes in orientation and aspect ratio (below)



would take *deliberate actions* in image-processing software, *and could not have been due to inadvertent error*.



#### J. Dr. Wang Supplies Doctored Images in March 29, 2022 *Neuroscience* “Corrigendum”

419. In October 2021, Dr. Bik raised concerns regarding **Figures 4** and **7** in Dr. Wang’s 2021 paper “Stress Diminishes BDNF-stimulated TrkB Signaling, TrkB-NMDA Receptor Linkage and Neuronal Activity in the Rat Brain,” in *Neuroscience*. She wrote that in **Figure 7** there were “remarkable similarities in shapes and background shading of” certain bands and in **Figure 4B** certain panels “look[] similar” to a panel in **Figure 7B**.



420. On March 29, 2022, the journal *Neuroscience* reported that the authors provided a “Corrigendum” validating Dr. Bik’s concerns. It stated:

The authors regret that *two errors pertaining to the visual display of representative western blot images were made during the generation of Fig. 4A and Fig. 7*. In Fig. 4A, an incorrect image of six protein bands was inserted instead of the correct Erk2 band (lower band). In Fig. 7A, the  $\beta$ -actin bands was placed in the incorrect orientation (bottom band).

Yet the authors also claimed that “[t]hese two honest human errors have no material impact on the findings of the research (the data analyses are correct) and instead relate to the visual display of representative western blots.” The authors further claimed they provided “[t]he corrected versions of Fig. 4A and 7A” and, “[t]o show the integrity of bands in Fig. 4A, Fig. 6E and Fig. 7A, the original uncropped blots” were also supposedly provided.

421. Upon closer inspection by Dr. Bik, however, she wrote that “[t]he ‘uncropped’ blots in the correction *do not appear to be uncropped blots*” and that “I do not see any marker lanes, or edges of the blots. According to the methods, the signal was detected using chemiluminescence, using an X-ray film. Could the authors please show the original films?” In addition, the concerns regarding the similarities in panels of **Figures 4B** and **7B** were not addressed in the Corrigendum.

422. The next month, Dr. Bik raised additional concerns with the “corrected” images, specifically that: “the molecular weight sizes of the proteins on the ‘uncropped’ blots provided for Figures 4 and 7 also do not seem to match that of the individual blot panels shown in the publication.” Dr. Bik described that, first, “[t]he uncropped blot for Figure 4A shows PSD95 (100 kDa), pAkt1 (55 kDa), and ERK2 (55 kDa). The pAkt1 and ERK2 bands should run at the same size, but they are shown far apart.” Second, “[t]he uncropped blot for Figure 7A shows TrkB (130 kDa), Akt1 (55 kDa), and b-Actin (55 kDa). The Akt1 and b-Actin bands should run at the same size, but they are shown far apart.” She asked: “Are the authors really sure that these ‘uncropped’ blots are the correct ones?”

**K. The March 30, 2022 Retractions in *PLOS One***

423. On March 30, 2022, *PLOS One* retracted *five* papers published by Drs. Wang and Burns, including their 2008 paper “High-Affinity Naloxone Binding to Filamin A Prevents Mu Opioid Receptor-Gs Coupling Underlying Opioid Tolerance and Dependence” criticized in the Citizen Petition, and their 2009 paper “Naloxone’s Pentapeptide Binding Site on Filamin A Blocks Mu Opioid Receptor-Gs Coupling and CREB Activation of Acute Morphine.”<sup>14</sup> For each of the five papers, the journal stated: “The data and comments provided to PLOS *did not resolve the concerns about the integrity and reliability of the reported data*. In light of these issues, the PLOS ONE Editors retract this article.”

424. And for each of the five retracted papers, Drs. Wang and/or Burns “provided image data to support the contested western blot results” but “[p]er PLOS’ assessment of the data files, the pixel patterns in background areas of blot images provided for multiple panels in [1-5] *appear more similar than would be expected for data obtained in independent experiments*.” Furthermore, the retraction noted “the supporting data files *did not contain positive controls as needed to verify the reliability of the results*.”<sup>15</sup> Drs. Wang and Burns did not agree with the retractions and provided additional excuses, claiming the “repetitive features” were due to “background noise of the image data are likely the result of scanner artifacts.” The journal, however, concluded that the “explanation given for the background image similarities *does not resolve the journal’s concerns in light of PLOS’ assessment of the data files*.”

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<sup>14</sup> In addition, the journal retracted three other papers published by Dr. Wang: “Prenatal Cocaine Exposure Increases Synaptic Localization of a Neuronal RasGEF, GRASP-1 via Hyperphosphorylation of AMPAR Anchoring Protein, GRIP” (2011); “Prenatal Cocaine Exposure Uncouples mGluR1 from Homer1 and Gq Proteins” (2014); “Prenatal Cocaine Exposure Upregulates BDNF-TrkB Signaling” (2016).

<sup>15</sup> As Dr. Burns wrote in a September 20, 2021 email to *Neuroscience’s* Dr. Gomez, obtained pursuant to a FOIL request, Dr. Wang “handed over all electronic files for an investigation” and did not have access to them. It therefore appears likely that Dr. Burns was also involved in providing information to journals in response to their inquiries following the publication of the Citizen Petition.

**L. Numerous Alzheimer’s Disease Experts Corroborate the Citizen Petition in an April 18, 2022 *New York Times* Exposé**

425. For its April 18, 2022 exposé, “Scientists Question Data Behind an Experimental Alzheimer’s Drug,” *The New York Times* “contacted nine prominent experts for comment about the scientific underpinnings of Cassava’s trials. *All said they did not trust the company’s methods, results or even the premise* underlying the drug’s supposed effectiveness.”

426. Dr. Nicoll, previously interviewed in connection with *The New Yorker* article, said he was particularly angered that Cassava’s work is partly funded by taxpayers. In all, the Company has received more than \$20 million from the NIH. ““This drug should not be put into patients. It should never have been. *Never*,’ he added. ‘The longer this goes on, the more outraged I am.’”

427. In the article, Barbier continued to deny any misconduct, without providing information rebutting the allegations leveled against the Company, instead complaining that “many of Cassava’s critics were ‘bad actors’ with financial conflicts of interest,” and that “the allegations of data manipulation were false.” And despite the meritorious concerns raised by scores of outside experts, Barbier wrote in an email: ““We stand by Professor Wang 100 percent.””

428. But the Alzheimer’s experts interviewed in the article said they knew of no independent studies that supported Cassava’s hypothesis that simufilam restores the normal shape and functioning of filamin A thereby slowing dementia, or would explain the Company’s results. ““The overall conclusions with regard to Alzheimer’s disease *make no sense to me whatsoever*,’” said Dr. Südhof, the Stanford professor and Nobel laureate. While Cassava claims that its theory is supported by strong evidence in its studies, ““in fact, all the evidence seems to be from [Dr. Wang’s] lab,”” said Dr. Lawrence Honig, an Alzheimer’s disease expert at Columbia. And ““[i]f the data is suspect in key papers, and not just minor mistakes, *you can’t trust anything*,’” said Dr. George Perry, a neuroscientist at the University of Texas at San Antonio and editor in chief of *The Journal of Alzheimer’s Disease*, who serves on the boards of companies with other drug candidates. ““It’ll have to be independently validated,”” he added. Indeed,

while irregularities or errors in one or two images could be due to chance, “***when you see it again and again, it makes it unlikely that you could do it accidentally,***” said Dr. David Vaux, deputy director of scientific integrity and ethics at the Walter and Eliza Hall Institute of Medical Research in Australia. Dr. Bik said that the problematic images she highlighted from the Citizen Petition along with the additional problematic images she uncovered that appear to show that results had been copied and pasted from other experiments “were of ***severe concern,***” and that “[b]ased on the ***pattern of irregularities*** in images in multiple papers, she believes ‘it is ***highly likely*** that there was some manipulation going on.’”

429. In addition, the experts pointed to several methodological “oddities” in the Company’s work. For example, as highlighted in the Citizen Petition, Cassava points to changes in the levels of certain molecules in cerebrospinal fluid, or CSF, as evidence of simufilam’s effectiveness. But, as the Citizen Petition and *The New York Times* revealed, the levels that the Company reported are “out of range for the testing method that was used,” according to Dr. William Hu, an expert on spinal fluid markers at Rutgers who works with a number of companies that develop such assays. One marker of inflammation was “much higher than is typically reported for Alzheimer’s disease patients, he added. ‘There’s a ***clear discrepancy*** there for those of us who work with C.S.F. biomarkers,’ Dr. Hu said. ‘That type of discrepancy ***really raises questions in terms of the rigor as well as the reliability of these results.***’”

430. In another set of experiments, Cassava reported data suggesting that its drug was able to restore the shape of most of the filamin A protein in the brain [in the 2017 *Neurobiology of Aging* paper “PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer’s disease pathogenesis”] – “a dramatic recovery that Dr. Südhof . . . questioned ‘There’s just ***no possibility, no rational way this could happen,***’” he said. He added that Cassava’s theories “‘seem implausible and contrived.’”

431. Dr. Vaux and other experts *The New York Times* interviewed also explained “the limitations of peer review in identifying mistakes or manipulation, and said many scientific journals are

reluctant to retract papers because of their fear of being sued, or damage to their own reputations.” “‘It’s time for regulatory bodies to step in, as it seems that the peer review process has taken it as far as it can,’ Dr. Hu said.”

432. On this news, Cassava’s stock price fell 11.3%, or \$4.92 per share, on April 19, 2022, to \$22.46 per share, and continued falling the following day another 9.2%, to \$20.39 per share, on April 20, 2022.

**M. The June 1, 2022 Retraction in *Alzheimer’s Research & Therapy***

433. On June 1, 2022, the journal *Alzheimer’s Research & Therapy* retracted a 2017 paper published by Dr. Wang and others, entitled “Increased A $\beta$ 42- $\alpha$ 7-like nicotinic acetylcholine receptor complex level in lymphocytes is associated with apolipoprotein E4-driven Alzheimer’s disease pathogenesis.” The retraction noted:

Following publication, concerns have been raised regarding the western blot images presented in Figs. 1, 5 and 6. The authors have provided the raw data, which have been assessed by independent experts and *deemed insufficient to address the concerns*. The Editors-in-Chief therefore *no longer have confidence in the integrity of the data in this article*.

As in prior instances, the purported “raw data” was “insufficient to address the concerns.”

434. On this news, Cassava’s stock price fell 12.4%, or \$3.78 per share, on June 1, 2022, to \$26.82 per share.

**N. A July 27, 2022 *Reuters* Article Reveals a Criminal Investigation Into Cassava**

435. On July 27, 2022, *Reuters* published a story revealing that the DOJ “opened a criminal investigation into Cassava . . . involving whether the biotech company manipulated research results for its experimental Alzheimer’s drug.” According to the news outlet, “[t]he [DOJ] personnel conducting the investigation into Austin, Texas-based Cassava specialize in examining whether companies or individuals have misled or defrauded investors, government agencies or consumers.”

436. In the article, Cassava, through an attorney, continued to deny any wrongdoing, stating: ““To be clear: Cassava Sciences vehemently denies any and all allegations of wrongdoing.”” According to Reuters, the criminal investigation began “sometime after [the Citizen Petition] was filed in August 2021.”

437. On this news, Cassava’s stock price fell 14%, or \$3.03 per share, on July 27, 2022, to \$18.69 per share.

## **X. ADDITIONAL SCIENTER ALLEGATIONS**

### **A. Defendants Knew or Were Reckless in Not Knowing that Cassava’s Pre-clinical and Clinical Data had been Manipulated**

438. As alleged herein, Cassava and the Individual Defendants acted with scienter in that they: (i) knew that the public documents and statements issued or disseminated in the name of the Company were materially false and misleading; knew that such statements or documents would be issued or disseminated to the investing public; and (ii) knowingly and substantially participated or acquiesced in the issuance or dissemination of such statements or documents as primary violations of the federal securities laws. As set forth herein in detail, the Defendants, by virtue of their receipt of information reflecting the true facts regarding Cassava, their control over, and/or receipt and/or modification of Cassava’s allegedly materially misleading statements and/or their associations with the Company which made them privy to confidential proprietary information concerning Cassava, participated in the fraudulent scheme alleged herein.

439. Defendants knew or were reckless in not knowing that Cassava’s pre-clinical and clinical research on simufilam had been manipulated. Their direct involvement in and focus on the development of simufilam and its pre-clinical research and clinical trial results evidences their knowledge that the data in that same pre-clinical research and clinical trials had been manipulated.

440. Cassava’s primary product candidate is simufilam. The Company makes no other products and has no revenue; the development of simufilam is therefore Cassava’s primary business. And a “[k]ey” element of Cassava’s business strategy to develop simufilam as a treatment for neurodegeneration included

*“validating our unique scientific approach with competitive research grants and publishing our scientific data in peer-reviewed journals.”* Moreover, between 2012 and 2019 Cassava had just eight to nine employees, and by year-end 2020, Cassava had just 11 full time employees. The four Individual Defendants, Barbier, Burns, Friedmann, and Schoen, alone made up as much as nearly half the Company when many of the alleged manipulations of the Company’s data were taking place.

441. Barbier and Drs. Burns and Friedmann, moreover, had direct responsibility overseeing simufilam’s development and the pre-clinical research and clinical trial results alleged to have been manipulated, and even *authored the research that is alleged to have been manipulated*. Barbier is a member of Cassava’s product development team and has “global responsibilities for the scientific direction, management, operations, strategy, and financing of the Company.” He has publicly bragged: “*I know* the science, *I know* the data.” Barbier is indeed listed, along with Drs. Wang, Burns and Friedmann, as an author of Cassava’s 2020 paper “PTI-125 Reduces Biomarkers of Alzheimer’s Disease in Patients,” published in the *Journal of Prevention of Alzheimer’s Disease*, that reports the results of the Company’s Phase 2a trial in simufilam, which are alleged to be false and misleading. The *JPAD* paper explicitly states that Cassava “monitored the conduct of the study and data collection.”

442. Barbier is also *married* to Dr. Burns, a senior vice president at Cassava and another member of its management and product development teams, who is in charge of Cassava’s Alzheimer’s program and co-authored each of the “key” pre-clinical and clinical research papers funded by Cassava supporting simufilam’s development alleged to have been manipulated. Dr. Burns describes herself as the “project leader on [Cassava’s] Alzheimer’s program” since the time her “academic collaborator, [Dr. Wang], identified filamin A (FLNA) as a novel therapeutic target.” Dr. Burns has even acknowledged she “*monitored* the proof-of-concept research, lead selection and efficacy experiments for PTI-125 and *oversaw* IND-enabling studies, chronic toxicity studies, and first-in-human and first-in-patient clinical trials.”



443. Dr. Burns also authored the Cassava presentations containing the manipulated data alleged to be false and misleading, such as the November 7, 2020 Conference on Clinical Trials on Alzheimer’s Disease slide deck entitled “Sumifilam [*sic*] Significantly Improves Eleven CSF Biomarkers in a Randomized, Placebo-controlled, One-month Clinical Trial in Alzheimer’s Disease Patients,” which also included Drs. Friedmann and Wang as co-authors, concerning Cassavas Phase 2b results; and the July 26, 2021, Cassava Sciences poster presented at the AAIC, entitled “SavaDx, a Novel Plasma Biomarker to Detect Alzheimer’s Disease, Confirms Mechanism of Action of Simufilam” regarding their Phase 2b trial results, which included Dr. Wang as a co-author.

444. Dr. Burns’s frequent co-author and “co-lead scientist on discovery & development of PTI-125,” Dr. Wang, is Cassava’s principal scientific advisor, and he conducted research and laboratory work with Dr. Burns directly for the Company for over a decade. In addition to Cassava’s published pre-clinical research and clinical trial results, Dr. Wang is also included as an author on various Company presentations press released or filed by Cassava with the SEC on Form 8-K alleged to be false and misleading in ¶¶283-284; 312-314, above. Together, the Citizen Petition’s analysis of Drs. Wang’s and Burns’s published journal manuscripts shows a series of anomalies that suggest a 15-year *pattern of systematic data manipulation and misrepresentation in virtually every publication* underlying Cassava’s simufilam claims.

445. Finally, Dr. Friedmann is described in documents submitted to the NIH by Cassava as “overseeing the clinical development” of simufilam, and he is a member of the Company’s management and development teams. He also co-authored the Company’s false and misleading presentations, listed in ¶¶268; 283-284; 292 above, that Cassava press released or filed with the SEC on Form 8-K. In sum, due to their direct involvement in overseeing the research and trial results alleged to be false and misleading, Defendants knew, or were reckless in not knowing, of the manipulations and anomalies in that data.

**B. Defendants Intentionally Manipulated Cassava’s Pre-Clinical and Clinical Data**

446. The extensive evidence of data manipulation detailed in the Citizen Petition, and confirmed by independent experts, demonstrates a pattern of *intentional* scientific misconduct that undermines the foundational science related to simufilam as a treatment for Alzheimer’s disease.

447. After the problems with Cassava’s research were raised in the Citizen Petition, Dr. Vaux, the Deputy Director of Science Integrity and Ethics at the Australian Walter and Eliza Hall Institute of Medical Research stated in *Retraction Watch*: “It is *not conceivable* that features in the images (such as apparent duplications) arose due to coincidence (chance) or accident, leaving the only plausible explanation being that the images were *deliberately* falsified or fabricated.”

448. Dr. Bik similarly stated that “[b]ased on the *pattern of irregularities* in images in multiple papers,” it is “*highly likely* that there was some manipulation going on.”

449. Dr. Rossner, too, found that many of the alleged manipulations or duplications *have the hallmarks of deliberate actions* using image-processing software, and, thus, do not appear to be the results of inadvertent error on the part of the authors.

450. As detailed at ¶¶105-109; 122-128; 137; 140-141; 146-152; 155-190; 200-216; 237-240; 338-362; 386-407; 425-428, evidence of these intentional acts includes image panels that were falsified by duplicating individual bands using image-processing software, similarities in images that could not have occurred by chance, and deliberate actions in image-processing software that could not have been due to inadvertent error.

**C. Defendants’ Submission of False Data to Journals to Obtain Exculpatory Statements Is Indicative of Scienter**

451. Defendants’ scienter is also evidenced by the attempts to cover-up their deceptive and fraudulent activities. As set forth in ¶¶338-362; 386-407, Drs. Burns and Wang attempted to present manipulated images to journals as original data when those journals began investigating the Citizen

Petition’s revelations in an attempt to cover up Defendants’ fraud and obtain exculpatory statements from those journals that data manipulation had not taken place. Cassava, Barbier, and Schoen then used those exculpatory statements to issue Company press releases falsely suggesting that there had been no scientific misconduct in Cassava’s pre-clinical research papers.

452. Yet, as the November 17, 2021 supplement to the Citizen Petition concluded: “The bottom line is Cassava Sciences **does not** appear to have provided the Journal of Neuroscience ‘original, uncropped Western blots’ as represented in its 11/4/2021 press release, so the journal could not have exonerated them, as they so dramatically suggested.” Rather, “the company appears to have **knowingly** taken the published image (the one of the left above), blurred it a bit, and then photoshopped it onto a slightly different canvas to ‘create’ the image on the right.” Notably, the *Journal of Neuroscience* changed its initial Editorial Note into an Expression of Concern after Dr. Bik provided evidence that that so called “original” data had itself been manipulated.

453. And, as Dr. Rossner concluded regarding the “original” images Drs. Wang and Burns provided in the December 20, 2021 *Neuroscience* Editorial Note, **all** of the images provided in the December 20, 2021 Editorial Note were cropped images and not full scans. Thus, **they do not constitute the original source data**, as claimed in the Editorial Note. Dr. Rossner indeed found evidence that the so called “original” data had itself been manipulated, altered using image processing software and duplicated.<sup>16</sup>

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<sup>16</sup> On August 18, 2022, the Company issued a press release reporting that the *Journal of Prevention of Alzheimer’s Disease* had purportedly provided the following statement: “‘We have completed our review of your article “PTI-125 Reduces Biomarkers of Alzheimer’s Disease in Patients” (JPAD 2020;7(4):256-264). We do not find convincing evidence of manipulation of data or intent to mislead, and therefore take no action regarding the published paper.’” The statement did not say, however, that any original data had been provided to the journal. Nor did the journal’s statement address the abnormalities found in the biomarker data detailed herein. Indeed, the market did not react favorably to the press release. In response, the Company’s stock price closed at \$26.47, **down** from the Company’s \$30.05 opening price that day.

**D. Cassava’s Failure to Disclose Dr. Wang’s Involvement with the Phase 2b Clinical Trial is Contrary to Barbier’s Own Statements and the Company’s Prior Disclosures**

454. Barbier’s scienter is further demonstrated by his failure to follow his own standards regarding disclosing conflicts of interest. Barbier himself considers failures to disclose such conflicts significant. In an April 26, 2022 public letter to *The New York Times* criticizing a purported lack of disclosure regarding conflicts of interest in the newspaper’s April 18, 2022 article about the Company, Barbier rhetorically asked wouldn’t a “reasonable” person want to know if “consulting experts made money, or stand to make money” because “[t]hese questions matter. They matter because without clear, full disclosures around competing interests,” people “may have bought into an agenda of profiteers.” He further noted that “[s]cience journals require full disclosure of all financial, consulting, and personal relationships that could be viewed as a potential conflict of interest.” But Cassava failed to make such disclosures in connection with announcing the results of the Company’s controversial reanalysis of its Phase 2b data on September 14, 2020. Instead, Cassava misleadingly described the lab conducting the Phase 2b reanalysis as an “outside” lab and failed to disclose Dr. Wang’s involvement or any of the conflicts that Dr. Wang had in conducting that analysis, including his involvement in a Company bonus plan.

455. When journalists at *The New Yorker* later asked Barbier whether it was appropriate for Dr. Wang to be included in a bonus plan based on short term fluctuations in Cassava’s stock price, Barbier said that this was standard practice. But when the same question was posed to Bob Gussin, a former Johnson & Johnson executive who sits on Cassava’s Board, and he stated: “‘It’s not typical, I’ll say that. And I’m not thrilled with that aspect of things.’”

456. In fact, Cassava’s failure to disclose Dr. Wang’s involvement in the Phase 2b reanalysis was also *inconsistent* with the Company’s prior practice. In a prior disclosure, Cassava revealed that Dr. Wang and his lab at CUNY were conducting specific experiments for Cassava. Cassava’s December 6,

2019 Form 8-K attaching the December 5, 2019 “Cassava Sciences, Inc. presentation at the 12th International Conference on [CTAD] on December 5, 2019” regarding the Company Phase 2a results, included a “Disclosures and Contributions” section which disclosed that Dr. Wang was a consultant to Cassava and that he and others at CUNY “performed the biomarker assays and are affiliated with the [CUNY] School of Medicine.” But Defendants hid that fact when it came to Cassava’s controversial reanalysis of their initially unsuccessful Phase 2b trial results.

#### **E. Defendants’ Reckless Failure to Investigate**

457. Cassava’s repeated denials regarding the Citizen Petition’s claims were made recklessly and without a sufficient attempt to verify whether the allegations of image manipulation and falsification were true, despite that numerous independent experts, including Dr. Bik, came forward to confirm that the petition had merit. Rather than investigating the Citizen Petition’s claims, Cassava, as Dr. Bik noted in a November 23, 2021 *Fierce Biotech* article, released its August 25, 2021 statement denying the petition’s claims:

Basically, they called all these allegations fiction, and then they had facts, and *some of these facts were clearly, in my opinion, fiction*, and it was *not written by a person who had any knowledge about molecular biology or about blots in general*. It was very dismissing of all the concerns, while, in my opinion, the *concerns had merit*.

458. In a September 3, 2021 “public statement,” however, Barbier agreed that “[o]ne way to settle the discourse around Western blots might be to go back to the original films and images.”<sup>17</sup> But Barbier has never provided the original films and images to Dr. Bik or the public more generally or released the results of any independent analysis of the original data to dispel these concerns. He instead claimed “we *don’t have* the original films or images for the Western blots in question” and that “[t]hose were generated by our science collaborator at CUNY, who is Prof. Wang,” thus confirming that Cassava had undertaken no investigation in whether certain images in the published works had been manipulated or

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<sup>17</sup> September 3, 2021, “Public Statement Regarding Recent Allegations Against Cassava Sciences, Inc.” at 5.

falsified. Barbier has never provided an explanation as to why, with the integrity of his Company, personnel and research being called into question, Cassava did not request the original images from CUNY to resolve the concerns.

459. Barbier has rather continued to emphasize and defend Cassava's longstanding relationship with Dr. Wang, telling investors:

Prof. Wang has also been a scientific collaborator to Cassava Sciences for about 15 years on the Alzheimer's program. Over 15 years, you get to know someone very well. Based on our long-term scientific relationship with Prof. Wang, we support his scientific integrity and ethics in the strongest possible terms.

460. Moreover, the September 9, 2021 Citizen Petition supplement called Barbier's claim that Cassava has no original data "highly doubtful," pointing out that "Dr. Burns, a Cassava employee and his wife, is the corresponding author for this phase 2a biomarker 2020 paper in the *Journal of Prevention of Alzheimer's Disease* (doi: 10.14283/jpad.2020.6)," and "[a]s corresponding author, Dr. Burns is **responsible** for storing, maintaining, and validating any data after publication and as a company conducting a clinical trial Cassava is responsible for storing these original phase 2a data and relevant records."

461. Indeed, a June 15, 2021 draft of a Cassava Investigational Research Agreement from CUNY includes a data retention policy, which states: "All data generated in the Research, including all information required in the Protocol, records, reports, and other work product generated by or on behalf of Researcher in the course of performance of the Research ('Data') **shall be the sole and exclusive property of Cassava.**"

462. The agreement further states:

All Data collected under the Protocol **shall be delivered to Cassava** by Investigator in a timely manner throughout the performance of this Research, as provided in the Protocol, and in no event later than ten (10) working days after the date of termination of this Agreement or on which Cassava otherwise requests delivery of the Data. **Cassava shall have the right to review, publish, disclose and use, any Data developed during the course of this Research** as Cassava, in its sole discretion, deems appropriate, including, without limitation, in submission to FDA and other regulatory authorities.

463. Neither Barbier nor Cassava explained why the Company would not also retain the data and materials from the pre-clinical and clinical research that Cassava funded and maintained as confidential under agreements signed by the Company’s scientific collaborators and advisors to protect Cassava’s “proprietary information and the results of studies conducted at our request.” Barbier’s claim is also suspect given Dr. Burns’s involvement in providing data to those journals investigating image manipulation claims following the release of the Citizen Petition.

464. In any case, that Cassava might not have the original images provides no defense to their failure to properly investigate. Pursuant to principals outlined by the Office of Research Integrity for the United States Department of Health and Human Services, “[a]uthentication of a scientific image *requires* access to the original data.” And importantly, “in the case where an image lacks authenticity, the *absence of the original data can be used as evidence of possible research misconduct* and sufficient justification to conduct further fact finding.” Defendants’ failure to authenticate the original data before publicly denying the veracity of the Citizen Petition was itself reckless, especially given the response from the scientific community that the Citizen Petition’s claims were valid.

## **F. Motive and Opportunity**

### **1. Accruing Cash Bonuses Worth Hundreds of Millions of Dollars**

465. As set forth in ¶¶98-104, the Individual Defendants were motivated to materially misstate the pre-clinical and clinical research for simufilam’s continued development to increase their personal wealth by the terms of their suspiciously timed executive bonus plan.

### **2. Funding the Individual Defendants’ Bonus Pool and the Company’s Continued Operations**

466. Cassava repeatedly informed investors that the Company would need to continue to raise capital to fund its operations. The Company had long experienced significant operating losses and warned investors that it expected to continue to incur substantial additional operating losses for years in the future. Obtaining financing to support the Company’s operations was critical.



467. With no material source of revenue in the foreseeable future and increased clinical trial expenses mounting, Cassava's continued existence as a going concern relies on the amount of capital it can raise through public and private offerings. As a consequence, and following their Class Period false and misleading statements, Defendants launched a series of offerings to fund the Company's continued operations.

468. A month after Cassava announced the results of its Phase 2b "re-do," which increased the Company's stock price over 100%, Cassava took advantage of the increase in its stock price and raised \$75 million in an underwritten public offering.

469. Then, a little over a week after Cassava's February 2, 2021 press release, which increased Cassava stock price by over 300%, the Company again cashed in, raising approximately \$200 million in a February 10, 2021 direct registered stock offering.

470. This funding was critical to Cassava's continuation as a going concern and the development of simufilam. In documents submitted to the NIH, Cassava acknowledged that the Phase 3 program would cost more than \$100 million and as much as \$200-\$300 million. Analyst at Cantor Fitzgerald also recognized in an October 22, 2020 report that Cassava's "\$25M in cash as of 2Q20" was "*not sufficient to conduct a large P3 study*, in our view."

471. During the September 14, 2020 call announcing the results of the Phase 2b trial reanalysis, Barbier further alluded to using the results to raise additional funds from investors, stating "I don't believe raising the money will be an issue for us" given the results to date. Schoen confirmed during the June 22, 2021 Raymond James Human Health Innovation Conference that the capital raise had been used to fund the phase 3 program, stating: "Cash on the balance sheet at the end of March, \$282 million, *that funds our Phase 3 program*." Barbier also stated in a September 3, 2021 statement that "[w]e raised capital from investors to fund the Phase 3 program."

472. But for Defendants’ alleged false and misleading statements, Cassava’s Class Period stock price would have been substantially lower, and Cassava would have been unable to raise \$275 million in cash.

473. In addition, Cassava suggested that the money raised in the February 10, 2021 offering may be used to pay the Individual Defendants’ bonuses. The February 12, 2021 Form 424(b)(b) Prospectus Supplement stated that “[w]e intend to use the net proceeds from this offering for working capital and general corporate purposes, including development of simufilam, our lead drug candidate for the treatment of Alzheimer’s disease,” and that,

while we do not have any current plans or understandings to do so, *we may also use a portion of the net proceeds from this offering for . . . payment of cash bonuses our board of directors may declare under our previously disclosed 2020 Cash Incentive Bonus Plan. We will have broad discretion in the application of any net proceeds we receive from this offering, and we could use any such proceeds for purposes other than those currently contemplated.*

474. Defendants also attempted to obtain “significant” funding from an unnamed source. During Cassava’s August 3, 2021 Q2 2021 earnings call, Barbier announced that “over the next few weeks or months, we expect to make a public announcement regarding an event that we think will result in significant multi-year capital inflows into Cassava Sciences.” Barbier further stated: “The expected capital inflows will be non-dilutive and non-debt. For obvious reasons, we cannot provide further guidance around this potential event until it occurs and is made public.” Following the publication of the Citizen Petition weeks later, however, this mysterious funding has never been realized.

## **G. Barbier’s and Friedmann’s Prior History of Making False and Misleading Statements**

### **1. Misleading Marketing Practices**

475. The FDA has previously chastised Pain Therapeutics, now Cassava, for “touting” an unapproved drug, their failed opioid painkiller, Remoxy. As reported in a September 16, 2016 STAT article, the FDA decided that Pain Therapeutics, and another company, were “touting an experimental drug

on their web sites in a way that appeared so misleading that the agency issued a rare letter to criticize their marketing practices.” As reported by STAT, according to the September 8, 2016 letter from the agency, which the FDA posted on its website, “the companies made statements that consumers might construe to mean the drug, Remoxy ER, is already approved for use. The agency pointed to certain language on the company websites – such as ‘long-acting’ and ‘tamper-resistant’ – that gave the impression these were ‘established facts’ pertaining to an approved drug.”

476. Moreover, according to the September 16, 2016 letter, as reported by STAT news,

the FDA believes the impact was magnified because the websites failed to clearly note that Remoxy ER is not yet approved, and referred to the medicine by the commercial name that would be used to market the treatment. And the agency complained that the design of the websites makes it difficult to find any of the few references to the experimental status of the drug, which is a form of oxycodone.

## 2. Prior Securities Fraud Class Action

477. This is also not the first time that Barbier, Friedmann, and the Company have been sued for securities fraud. Before Pain Therapeutics was re-branded as Cassava, investors filed a lawsuit against the Company, Barbier, and Friedmann in a securities class action in this District for concealing information from the public concerning the Remoxy FDA-approval process. Similar to the allegations at issue here, where Defendants concealed negative information concerning the development and prospects of their experimental drug while at the same time rewarding themselves with generous compensation packages, the plaintiff in that case claimed that, although the defendants knew they had failed to resolve problems with Remoxy’s stability that caused the FDA to reject the first Remoxy NDA, defendants led the public to believe those problems had been resolved while reapplying for FDA approval, and despite knowing the second NDA would also be rejected, defendants rewarded themselves with unjustifiable compensation packages they asked shareholders to approve.

478. That case, *KB Partners I, LP v. Pain Therapeutics, Inc., et al.*, A-11-CA-1034-SS (W.D. Tex. 2011), settled in 2016 on the eve of trial, but not before Senior United States District Judge Sam

Sparks ruled on summary judgment. On June 16, 2015, Judge Sparks issued a ruling denying defendants' motion for summary judgment, holding that the plaintiff had provided sufficient evidence that a jury could reasonably find that defendants made material misstatements and omissions with the requisite scienter.

479. Barbier's, Friedmann's, and the Company's pattern and history of making false and misleading statements further demonstrates their scienter here.

#### **H. Additional Knowingly False and Misleading Statements Defendants Made Regarding Cassava's Scientific Advisory Board**

480. For years, Cassava claimed in SEC filings, including in its March 23, 2021 Form 10-K, signed by Barbier and Schoen, that the Company's management team was "supported by scientific advisors that share our commitment to advancing new treatments for Alzheimer's disease." These "[l]eading experts in the field who advise[d]" Cassava purportedly included Dr. Wang and four others, including: (i) Barbara Sahakian, FBA, FMedSci, Professor of Clinical Neuropsychology at the Department of Psychiatry and Medical Research Council /Wellcome Trust Behavioral and Clinical Neuroscience Institute, University of Cambridge; and (ii) Steven E. Arnold, MD, Translational Neurology Head of the Interdisciplinary Brain Center, Massachusetts General Hospital, Harvard Medical School.

481. However, as Professor Sahakian wrote on Twitter on October 11, 2021: "I have not worked with Cassava *for years* and I never had shares in this company." The next month, Cassava deleted their Scientific Advisory Board link from their homepage.

482. And recently, Dr. Arnold told *The Daily Beast* in connection with its July 7, 2022 article, "Will This Drug Help Us Beat Alzheimer's? Or Will It Doom Its Makers Instead?," "There was only *one* formal advisory board meeting a few years ago,' *in 2018, before* Pain Therapeutics changed its name to Cassava Sciences . . . ."

483. Defendants' attempts to lend false legitimacy to their attempt to commercialize simufilam by overstating their scientific advisory board further demonstrates their scienter.

**I. Cassava’s Attempts to Remove Negative Information from the Internet Concerning the Company and Barbier’s Misleading Statements Concerning the FDA’s Response to the Citizen Petition**

484. Cassava has attempted to scrub negative information about the Company from the internet.

As reported in *Daily Beast’s* July 7, 2022 news story:

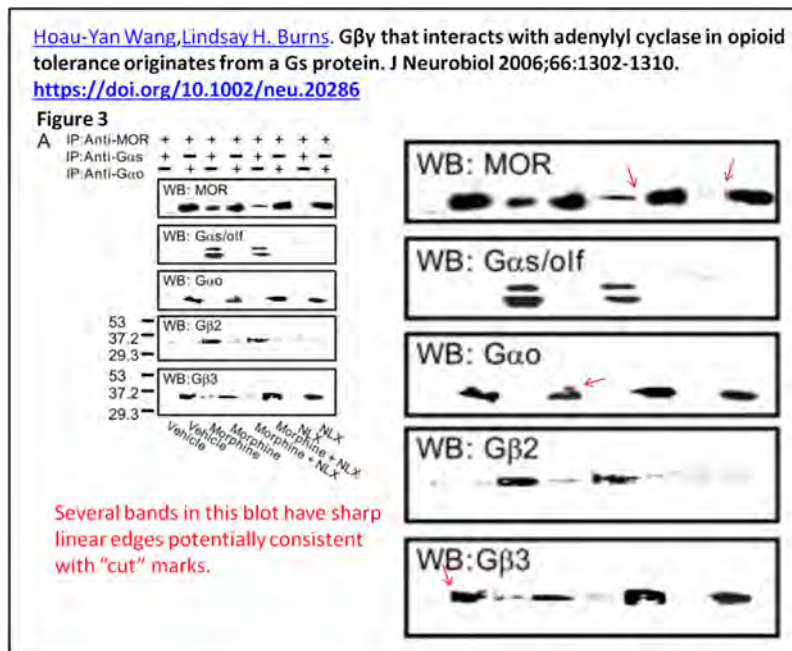
Cassava hasn’t sat quietly during these happenings. The Wikipedia pages for simufilam and for Burns have recently been edited by an IP address *originating from Cassava Sciences’ headquarters*. These changes included *removing* mentions of Burns being married to Barbier; dismissing alleged research misconduct because the papers in question were published in 2005 and “mostly unrelated”; and an addition that suggested the citizen’s petition was filed after the price of Cassava Sciences’ stock soared. Wikipedia editors flagged the changes for *policy violations and added that the user must disclose any conflicts of interest*.

485. Moreover, as detailed in ¶¶411-413, Barbier has continued to falsely inform investors that the FDA denied the Citizen Petition because the agency found no evidence of fraud, despite the fact that the FDA’s response letter stated no such thing, and rather specified that the petition was being denied “solely” on a technicality, which did “not represent a decision by the Agency to take or refrain from taking any action relating to the subject matter of your Petitions.”

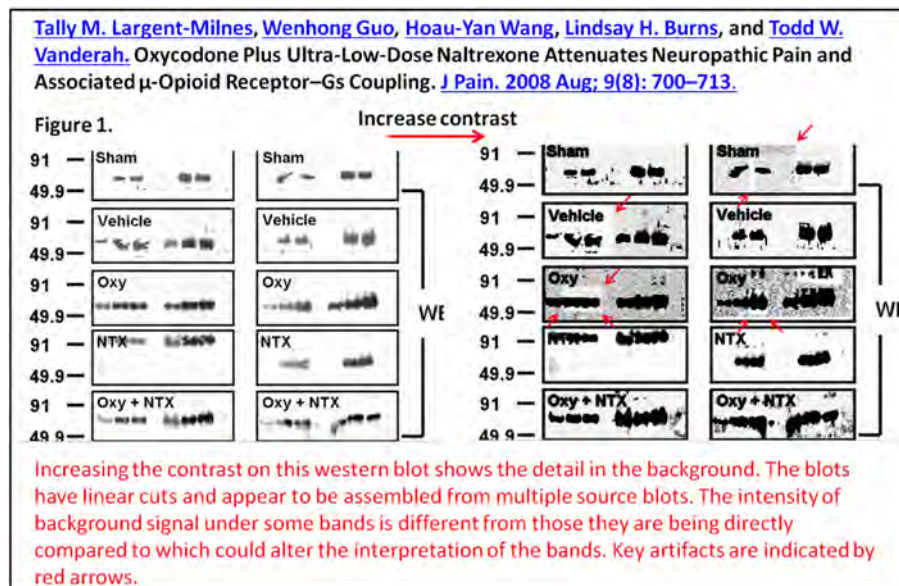
486. Cassava’s attempts to remove and misstate negative information about the Company’s misconduct and yet another failure to disclose a conflict of interest is indicative of Cassava’s and its executives’ scienter.

**J. Additional Data Manipulations Further Indicative of a Pattern and Practice of Deception**

487. In September 2021, a commenter on PubPeer identified “cut marks” indicative of splicing in **Figure 3** (below) in the 2006 paper “Gbetagamma that interacts with adenylyl cyclase in opioid tolerance originates from a Gs protein,” published by Drs. Wang and Burns in the *Journal of Neurobiology*.



488. Then, in November 2021, a commenter on PubPeer identified “significant anomalies” in the Western blots of **Figure 1** (below) in Drs. Wang’s and Burns’s 2008 paper published in *The Journal of Pain*, “Oxycodone Plus Ultra-Low-Dose Naltrexone Attenuates Neuropathic Pain and Associated  $\mu$ -Opioid Receptor-Gs Coupling.”



489. These additional manipulations in papers co-authored by Drs. Burns and Wang provided further evidence of their practice of data manipulation. The instances of data manipulations detailed herein



are not an exclusive list, but illustrative of their longstanding and systemic pattern of misconduct. Dozens of papers on which Dr. Burns and Wang are listed as an author, not all of which have been included here, have been identified as containing potential data duplication, manipulation and falsification.

**K. Quintessential Capital Management Report Detailing Questionable Practices at Cassava Clinical Trial Sites**

490. On November 3, 2021, Quintessential Capital Management (“QCM”), published a report (the “QCM Report”) disclosing their short position in Cassava based on an investigation it conducted into Cassava’s clinical trial sites. In the report, QCM arrived at the conclusion that

Cassava Sciences could be a scheme orchestrated by management to enrich itself at the expense of shareholders, patients, and the US Federal Government. The approval of an outrageous compensation policy, blatantly rewarding short term stock price appreciation (“pump & dump”) may have provided a clear incentive for management to engage in this reckless behavior.

491. QCM has investigated numerous companies in the past, and claimed that “our in-depth report named ‘A Parmalat in Bologna’ led to the collapse of the Italian €1.1 b-unicorn Bio-on S.p.A. and the arrest of the executives involved”; “our campaign against the Greek retailer Folli Follie led to the collapse and de-listing of the company in just three weeks”; and “our action against Aphria, a Canadian cannabis company with a market cap of more than \$4 billion, led to the immediate collapse of the stock and the dismissal of the entire board of directors,” among others.

492. The QCM Report, among other things, questioned Cassava’s association with and reliance on IMIC Inc. (“IMIC”), a clinical research center based in Palmetto, Florida hired by Cassava to conduct clinical trials, and its employees. These questionable individuals included: Aimee Cabo, president of IMIC, who was arrested for felony possession of cocaine; Evelyn Lopez-Brignoni, IMIC’s Principal Investigator for the simufilam trials at IMIC, who has received a FDA warning letter for “failing to ensure that the investigation was conducted according to the investigational plan” and for multiple serious infractions



related to a clinical trial she was overseeing at IMIC;<sup>18</sup> and Juana Pelegri, a purported “‘trained clinical psychologist’ [for IMIC] with expertise in diagnosing Alzheimer’s Disease” with no evidence, according to QCM, that she ever obtained a Ph.D. The QCM Report also highlighted that a senior clinical research associate at Pain Therapeutics from October 2018 to February 2019, Hilda Rodriguez, had previously been sentenced to two years in prison for felony theft in Texas.

493. Cassava’s association with such individuals, and reliance on IMIC as a clinical trial site, is further indicative of Defendants’ recklessness and scienter. The QCM report goes on to detail many questionable research practices being conducted at IMIC, including investigators from QCM being offered participation in a simufilam trial, *despite* being coached by QCM to pass a preliminary cognitive assessment test for entry into the study, such that the test would not reflect any significant cognitive issue, and therefore there would be no legitimate reason to include those investigators in an Alzheimer’s study.

## **XI. NO SAFE HARBOR**

494. The “Safe Harbor” warnings accompanying Cassava’s reportedly forward-looking statements (“FLS”) issued during the Class Period were ineffective to shield those statements from liability. Defendants are liable for any false or misleading FLS pleaded because, at the time each FLS was made, the speaker knew the FLS was false or misleading and the FLS was authorized and/or approved by an executive officer of Cassava who knew that the FLS was false. None of the historic or present tense statements made by Defendants were assumptions underlying or relating to any plan, projection or statement of future economic performance, as they were not stated to be such assumptions underlying or relating to any projection or statement of future economic performance when made, nor were any of the projections or forecasts made by Defendants expressly related to or stated to be dependent on those historic or present tense statements when made.

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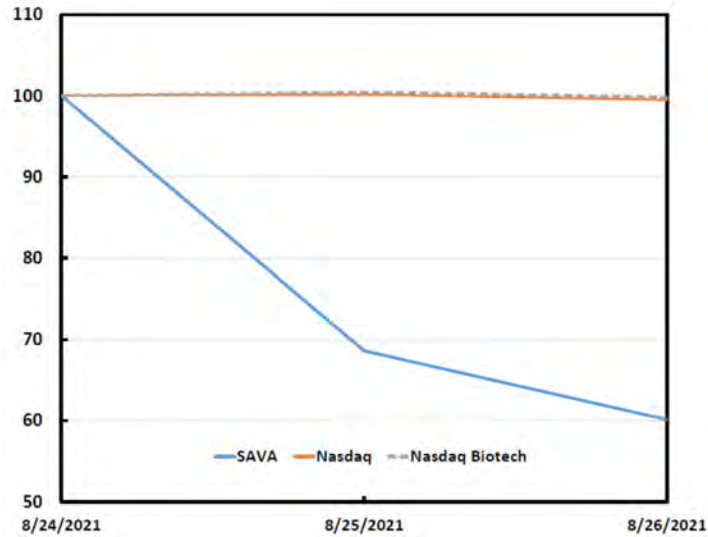
<sup>18</sup> The FDA warning letter is redacted and does not specify which clinical trial or trials the letter concerns or rule out a connection to Cassava.

## **XII. LOSS CAUSATION AND ECONOMIC LOSS**

495. During the Class Period, as detailed herein, Defendants engaged in a scheme to deceive investors and the market, and engaged in a course of conduct that caused Cassava securities to trade at artificially inflated prices and operated as fraud or deceit on Class purchasers or acquirers of Cassava securities by misrepresenting and omitting material information about the pre-clinical and clinical data supporting the continue development of the Company’s primary product candidate, simufilam. When Defendants’ prior misrepresentations and omissions were disclosed or otherwise leaked to the market, beginning on August 25, 2021, Cassava’s stock price declined significantly, as the prior inflation came out of the price. As a result of their purchases or acquisitions of Cassava securities during the Class Period, Plaintiffs and other members of the Class suffered economic loss, *i.e.*, damages, under the federal securities laws.

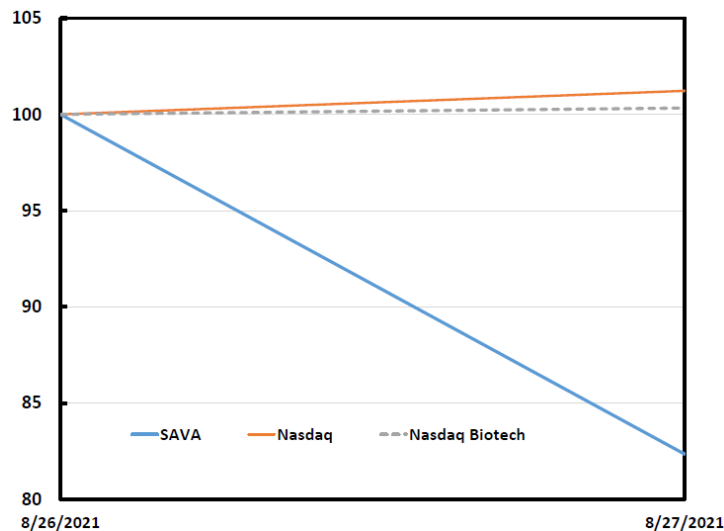
496. Defendants’ false and misleading statements and omissions, identified herein at ¶¶268-319; 338-343; 363-365; 386-389, had the intended effect and caused Cassava’s securities to trade at artificially inflated levels during the Class Period.

497. As a direct result of the disclosures and leakage that began on August 24, 2021, and are detailed in ¶¶12-15; 105-251; 316-318, Cassava’s stock price suffered a significant decline. As set forth in the chart below, between August 25, 2021 and August 26, 2021, the price of Cassava common stock traded on the Nasdaq dropped by \$46.98 per share, or 39.9%:



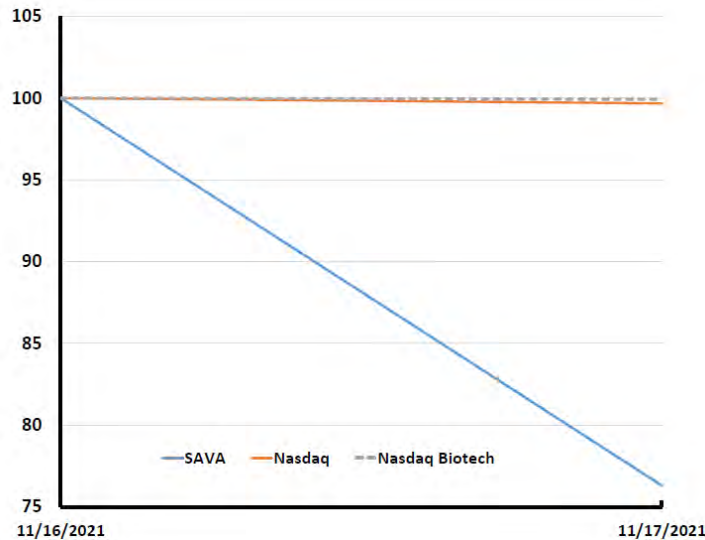
498. Comparatively, between August 25 and 26, 2021, the Nasdaq was down 0.5% and the Nasdaq Biotechnology Index was down just 0.2%.

499. The disclosures and leakage that began on August 27, 2021, detailed in ¶¶16-17; 323-327, also had a direct impact on Cassava's stock price. As set forth in the chart below, on August 27, 2021, the price of Cassava common stock dropped by \$12.51 per share, or 17.66%:



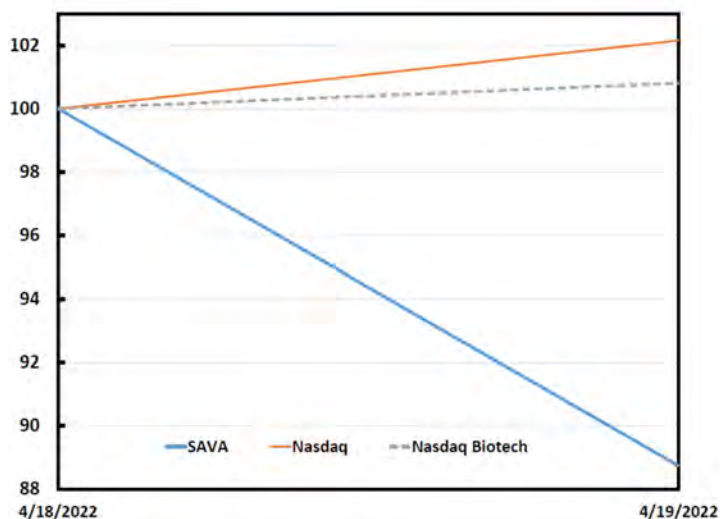
500. Comparatively, on August 27, 2021, the Nasdaq was up 1.23% and the Nasdaq Biotechnology Index was up 0.3%.

501. The disclosures and leakage that began on November 17, 2021, detailed in ¶¶28-30; 367-379, also had a direct impact on Cassava's stock price. As set forth in the chart below, on November 17, 2021, the price of Cassava common stock dropped by \$14.62 per share, or 23.7%:



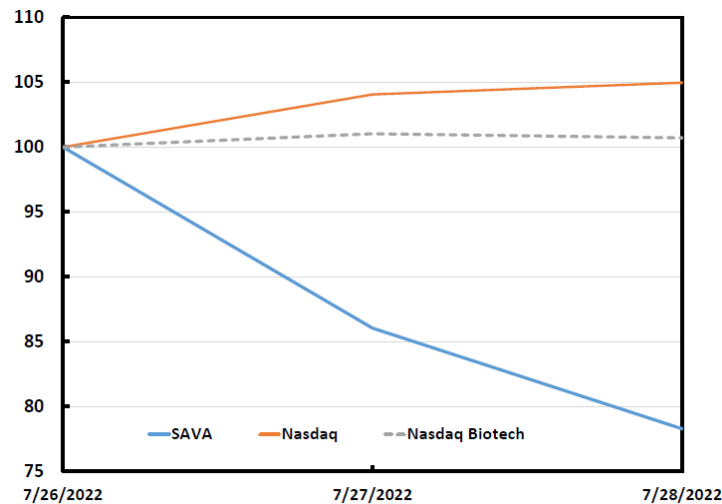
502. Comparatively, on November 17, 2021, the Nasdaq was down 0.33% and the Nasdaq Biotechnology Index was down just 0.1%.

503. The disclosures and leakage that began on April 18, 2022, detailed in ¶¶40-41; 425-432, also had a direct impact on Cassava's stock price. As set forth in the chart below, on April 19, 2022, the price of Cassava common stock dropped by \$2.85 per share, or 11.26%:



504. Comparatively, on April 19, 2022, the Nasdaq was up 2.15% and the Nasdaq Biotechnology Index was up 0.81%.

505. The disclosures and leakage that began on July 27, 2022, detailed in ¶¶ 44-45; 435-437, also had a direct impact on Cassava's stock price. As set forth in the chart below, on July 27, 2022, the price of Cassava common stock dropped by \$3.03 per share, or 14%:



506. Comparatively, on July 27, 2022, the Nasdaq was up 4.1% and the Nasdaq Biotechnology Index was up 1%.

507. The declines in Cassava's common stock price, set forth above, were a direct result of the nature and extent of Defendants' prior misstatements and omissions being revealed to investors and the market. The timing and magnitude of Cassava's stock price decline negate any inference that the losses suffered by Plaintiffs and other Class members were caused by changed market conditions, macroeconomic or industry factors or Company-specific factors unrelated to Defendants' fraudulent conduct.

508. The economic losses suffered by Plaintiffs and other members of the Class were a direct result of Defendants' fraudulent scheme to inflate Cassava's common stock price and the subsequent declines in the value of that stock when Defendants' prior misrepresentations and omissions were revealed.

### **XIII. SCHEME LIABILITY**

509. The Defendants engaged in a scheme to promote the continued development of an experimental drug using manipulated pre-clinical and clinical data and put profits over accurately reporting that data. This conduct caused the price of Cassava stock to trade at artificial levels during the Class Period, as the market was unaware that, in fact, the pre-clinical and clinical data supporting simufilam's continued development had been manipulated and that therefore the data supporting simufilam's efficacy, and Cassava's financial prospects, which are tied to simufilam's success, lacked integrity, reliability and had been overstated. Defendants engaged in this scheme to defraud by disseminating misleading statements to the investing public through the alleged false and misleading statements made in Cassava's SEC filings. Throughout the Class Period, each Individual Defendant prepared the pre-clinical and clinical research that is the subject of Defendants' misleading statements and/or the SEC filings on Forms 10-K, 10-Q, and 8-K containing the misleading statements knowing, or recklessly disregarding, they contained false and misleading statements that were to be disseminated to investors upon filing. Each Defendant is liable as a participant in this fraudulent scheme.

### **XIV. APPLICABILITY OF PRESUMPTION OF RELIANCE**

510. Plaintiffs and the Class are entitled to a presumption of reliance under *Affiliated Ute Citizens of Utah v. United States*, 406 U.S. 128 (1972), because the claims asserted herein against Defendants are predicated upon omissions of material fact for which there was a duty to disclose.

511. Plaintiffs and the Class are also entitled to a presumption of reliance pursuant to *Basic Inc. v. Levinson*, 485 U.S. 224 (1988), and the fraud-on-the-market doctrine because the market for Cassava stock were an efficient market at all relevant times by virtue of the following factors, among others:

(a) Cassava common stock met the requirements for listing, and was listed and actively traded on NASDAQ, a highly efficient market;

(b) Cassava regularly communicated with public investors via established market communication mechanisms, including the regular dissemination of press releases on the national circuits of major newswire services and other wide-ranging public disclosures, such as communications with the financial press and other similar reporting services; and

(c) Cassava was followed by a number of securities analysts who wrote reports which were distributed to the sales force and certain customers of their respective brokerage firms. These reports were publicly available and entered the public marketplace.

512. As a result of the foregoing, the market for Cassava stock promptly incorporated current information regarding the Company from publicly available sources and reflected such information in the prices of the stock. Under these circumstances, all those who transacted in Cassava securities during the Class Period suffered similar injury through their transactions in Cassava stock at artificially inflated prices and a presumption of reliance applies.

513. Without knowledge of the misrepresented or omitted material facts, Plaintiffs and other Class members purchased or acquired Cassava securities between the time Defendants misrepresented and failed to disclose material facts and the time the true facts were disclosed. Accordingly, Plaintiffs and other Class members relied, and are entitled to have relied, upon the integrity of the market prices for Cassava securities, and are entitled to a presumption of reliance on Defendants' materially false and misleading statements and omissions during the Class Period.

## **XV. CLASS ACTION ALLEGATIONS**

514. Plaintiffs bring this action on behalf of all purchasers or acquirers of Cassava securities during the Class Period who were damaged thereby (the "Class"). Excluded from the Class are Defendants and their immediate families, the officers and directors of the Company and their immediate families, their legal representatives, heirs, successors or assigns, and any entity in which any of the Defendants have or had a controlling interest.



515. The members of the Class are so numerous that joinder of all members is impracticable. Throughout the Class Period, Cassava common stock was actively traded on the NASDAQ. While the exact number of Class members is unknown to Plaintiffs at this time and can only be ascertained through appropriate discovery, Plaintiffs believe that there are hundreds or thousands of members in the proposed Class. Record owners and other members of the Class may be identified from records maintained by Cassava or its transfer agent and may be notified of the pendency of this action by mail, using the form of notice similar to that customarily used in securities class actions. Upon information and belief, these shares are held by hundreds or thousands of individuals located geographically throughout the country. Joinder would be highly impracticable.

516. Plaintiffs' claims are typical of the claims of the members of the Class as all members of the Class are similarly affected by Defendants' wrongful conduct in violation of the federal laws complained of herein.

517. Plaintiffs will fairly and adequately protect the interests of the members of the Class and have retained counsel competent and experienced in class and securities litigation. Plaintiffs have no interests antagonistic to or in conflict with those of the Class.

518. Common questions of law and fact exist as to all members of the Class and predominate over any questions solely affecting individual members of the Class. Among the questions of law and fact common to the Class are:

- (a) whether the federal securities laws were violated by Defendants' acts as alleged herein;
- (b) whether Defendants acted knowingly or with deliberate recklessness in issuing false and misleading statements;
- (c) whether the prices of Cassava common stock during the Class Period were artificially inflated because of Defendants' conduct complained of herein; and

(d) whether the members of the Class have sustained damages and, if so, the proper measure of damages.

519. A class action is superior to all other available methods for the fair and efficient adjudication of this controversy since joinder of all members is impracticable. Furthermore, as the damages suffered by individual Class members may be relatively small, the expense and burden of individual litigation make it impossible for members of the Class to individually redress the wrongs done to them. There will be no difficulty in the management of this action as a class action.

## **XVI. COUNTS FOR VIOLATIONS OF THE FEDERAL SECURITIES LAWS**

### **COUNT I**

#### **For Violation of §10(b) of the Exchange Act and Rule 10b-5 Against All Defendants**

520. Plaintiffs incorporate ¶¶1-519 by reference.

521. During the Class Period, Defendants disseminated or approved the false or misleading statements specified above, which they knew or recklessly disregarded were misleading in that they contained misrepresentations and failed to disclose material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading.

522. Defendants violated §10(b) of the Exchange Act and Rule 10b-5 in that they:

- (a) employed devices, schemes, and artifices to defraud;
- (b) made untrue statements of material fact or omitted to state material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading; or
- (c) engaged in acts, practices, and a course of business that operated as a fraud or deceit upon Plaintiffs and others similarly situated in connection with their purchases of Cassava common stock during the Class Period.

523. Plaintiffs and the Class have suffered damages in that, in reliance on the integrity of the market, they paid artificially inflated prices for Cassava securities. Plaintiffs and the Class would not have purchased or acquired Cassava securities at the prices they paid, or at all, if they had been aware that the market prices had been artificially and falsely inflated by Defendants' misleading statements.

524. As a direct and proximate result of Defendants' wrongful conduct, Plaintiffs and the other members of the Class suffered damages in connection with their purchases or acquisitions of Cassava securities during the Class Period.

## COUNT II

### **For Violation of §20(a) of the Exchange Act Against Barbier, Burns, Friedmann and Schoen**

525. Plaintiffs incorporates ¶¶1-524 by reference.

526. During the Class Period, Defendants Barbier, Burns, Friedmann and Schoen acted as controlling persons of Cassava within the meaning of §20(a) of the Exchange Act. By virtue of their stock holdings, positions and their power to control public statements about Cassava, Defendants Barbier, Burns, Friedmann and Schoen had the power and ability to control the actions of Cassava and its employees. Cassava controlled the Individual Defendants and its other officers and employees. By reason of such conduct, Defendants Barbier, Burns, Friedmann, and Schoen are liable pursuant to §20(a) of the Exchange Act.

## PRAYER FOR RELIEF

WHEREFORE, Plaintiffs pray for judgment as follows:

A. Determining that this action is a proper class action and certifying Plaintiffs as Class representatives under Rule 23 of the Federal Rules of Civil Procedure and Plaintiffs' counsel as Lead Counsel;

B. Awarding Plaintiffs and the members of the Class damages and interest;

C. Awarding Plaintiffs' reasonable costs, including attorneys' fees; and

D. Awarding such equitable/injunctive or other relief as the Court may deem just and proper.

### **JURY DEMAND**

Plaintiffs demand a trial by jury.

DATED: August 18, 2022

Respectfully submitted,

ROBBINS GELLER RUDMAN  
& DOWD LLP

DANIEL S. DROSMAN (*admitted pro hac vice*)

KEVIN A. LAVELLE (*admitted pro hac vice*)

NATALIE F. LAKOSIL (*admitted pro hac vice*)

MEGAN A. ROSSI

s/ Kevin A. Lavelle

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Counsel for Plaintiff Manohar K. Rao

CERTIFICATE OF SERVICE

I hereby certify under penalty of perjury that on August 18, 2022, I authorized the electronic filing of the foregoing with the Clerk of the Court using the CM/ECF system which will send notification of such filing to the email addresses on the attached Electronic Mail Notice List, and I hereby certify that I caused the mailing of the foregoing via the United States Postal Service to the non-CM/ECF participants indicated on the attached Manual Notice List.

s/ Kevin A. Lavelle

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# Mailing Information for a Case 1:21-cv-00751-DAE In Re Cassava Sciences, Inc. Securities Litigation

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## Manual Notice List

The following is the list of attorneys who are **not** on the list to receive e-mail notices for this case (who therefore require manual noticing). You may wish to use your mouse to select and copy this list into your word processing program in order to create notices or labels for these recipients.

- (No manual recipients)

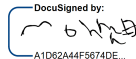
# EXHIBIT A

CERTIFICATION PURSUANT TO FEDERAL SECURITIES LAWS

Mohammad Bozorgi (“Plaintiff”) declares:

1. Plaintiff has reviewed a complaint and authorized its filing. Plaintiff has authorized the filing of a motion for appointment as lead plaintiff.
2. Plaintiff did not acquire the security that is the subject of this action at the direction of plaintiff’s counsel or in order to participate in this private action or any other litigation under the federal securities laws.
3. Plaintiff is willing to serve as a representative party on behalf of the class, including providing testimony at deposition and trial, if necessary.
4. Plaintiff has made the following transaction(s) during the Class Period in the securities that are the subject of this action: *See* attached Schedule A.
5. Plaintiff has not sought to serve or served as a representative party in a class action that was filed under the federal securities laws within the three-year period prior to the date of this Certification except as detailed below: None.
6. Plaintiff will not accept any payment for serving as a representative party on behalf of the class beyond the Plaintiff’s pro rata share of any recovery, except such reasonable costs and expenses (including lost wages) directly relating to the representation of the class as ordered or approved by the court.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct. Executed this 18<sup>th</sup> day of August, 2022.

DocuSigned by:  
  
A1D62A44E5674DE

Mohammad Bozorgi

**SCHEDULE A****SECURITIES TRANSACTIONS****Stock**

<b><u>Date Acquired</u></b>	<b><u>Amount of Shares Acquired</u></b>	<b><u>Price</u></b>
02/03/2021	4,400	\$76.81
05/28/2021	25,000	\$56.50
06/07/2021	25,000	\$65.35
06/11/2021	25,000	\$68.85
06/14/2021	25,000	\$78.70
06/22/2021	20,000	\$83.00
07/23/2021	10,000	\$120.00
07/26/2021	2,000	\$120.00
07/28/2021	5	\$132.00
07/29/2021	19,995	\$132.00
08/17/2021	5,000	\$110.00
08/19/2021	5,000	\$100.00
08/20/2021	5,000	\$103.00
08/24/2021	5,000	\$120.42
<b><u>Date Disposed</u></b>	<b><u>Amount of Shares Disposed</u></b>	<b><u>Price</u></b>
06/02/2021	5,982	\$57.50
06/03/2021	19,018	\$58.55
06/07/2021	25,000	\$67.00
06/11/2021	25,000	\$70.30
06/16/2021	10,000	\$78.21
06/21/2021	15,000	\$85.50
07/01/2021	19,400	\$90.00
07/23/2021	10,000	\$121.63
07/27/2021	2,000	\$127.26
08/11/2021	2,225	\$108.95
08/18/2021	5,000	\$111.00
08/19/2021	5,000	\$104.50
08/20/2021	5,000	\$101.00
08/30/2021	10,900	\$53.54
08/30/2021	550	\$53.10
09/14/2021	10,000	\$42.83
02/24/2022	4,325	\$36.10

Prices listed are rounded up to two decimal places.

# EXHIBIT B

**CERTIFICATION OF NAMED PLAINTIFF  
PURSUANT TO FEDERAL SECURITIES LAWS**

Kenneth W. Calderone ("Plaintiff") declares:

1. Plaintiff has reviewed a complaint and authorized its filing.
2. Plaintiff did not acquire the security that is the subject of this action at the direction of plaintiff's counsel or in order to participate in this private action or any other litigation under the federal securities laws.
3. Plaintiff is willing to serve as a representative party on behalf of the class, including providing testimony at deposition and trial, if necessary.
4. Plaintiff has made the following transaction(s) during the Class Period in the securities that are the subject of this action: *See* attached Schedule A.
5. Plaintiff has not sought to serve or served as a representative party in a class action that was filed under the federal securities laws within the three-year period prior to the date of this Certification except as detailed below: None.
6. Plaintiff will not accept any payment for serving as a representative party on behalf of the class beyond the Plaintiff's pro rata share of any recovery, except such reasonable costs and expenses (including lost wages) directly relating to the representation of the class as ordered or approved by the court.

I declare under penalty of perjury that the foregoing is true and correct.

Executed this 17<sup>th</sup> day of August, 2022.

  
Kenneth W. Calderone

**SCHEDULE A**

**SECURITIES TRANSACTIONS**

**Stock**

<b><u>Date Acquired</u></b>	<b><u>Amount of Shares Acquired</u></b>	<b><u>Price</u></b>
07/26/2021	200	\$125.99
07/29/2021	800	\$127.13

Prices listed are rounded up to two decimal places.



# EXHIBIT C

**SWORN CERTIFICATION OF PLAINTIFF****CASSAVA SCIENCES, INC. SECURITIES LITIGATION**

I, Manohar K. Rao, individually, and as assignee of the claims of Jyothi Rao and Shyamala Rambhotla, certify that:

1. Jyothi Rao and Shyamala Rambhotla have assigned to me all rights, title, ownership, and interest in claims, demands, and causes of action of any kind whatsoever that they have or may have arising from violations of the federal securities laws of the United States of America in connection with her purchase or acquisition of Cassava Sciences, Inc. securities.
2. I have reviewed the complaint in this action and authorize its filing.
3. The Cassava Sciences, Inc. securities that are the subject of this action were not purchased at the direction of plaintiff's counsel or in order to participate in any private action arising under this title.
4. I am willing to serve as a representative party on behalf of a class and will testify at deposition and trial, if necessary.
5. My transactions, including the transactions related to claims assigned to me, in Cassava Sciences, Inc. securities that are the subject of the complaint during the class period specified in the complaint are as follows:  
  
(See attached transactions)
6. I have not sought to serve, nor served, as a representative party on behalf of a class under this title during the last three years, except in this action.
7. I will not accept any payment for serving as a representative party, except to receive my pro rata share of any recovery or as ordered or approved by the court, including the award to a representative plaintiff of reasonable costs and expenses (including lost wages) directly relating to the representation of the class.

I declare under penalty of perjury that the foregoing are true and correct statements.

8/16/2022

Date

*Manohar K. Rao*

Manohar K. Rao

**Manohar K. Rao's Transactions in Cassava Sciences, Inc. (SAVA) Common Stock****Account 1**

<b>Date</b>	<b>Transaction Type</b>	<b>Quantity</b>	<b>Unit Price</b>
7/6/2021	Bought	50	\$92.6950
7/6/2021	Bought	50	\$90.7708
7/9/2021	Sold	-100	\$99.1621
7/19/2021	Bought	5,100	\$85.0000
7/19/2021	Bought	1,200	\$100.0000
7/23/2021	Sold	-200	\$121.3800
7/28/2021	Sold	-1	\$140.5200
7/28/2021	Sold	-10	\$140.7350
7/28/2021	Sold	-100	\$140.5320
7/28/2021	Sold	-100	\$140.5600
7/28/2021	Sold	-100	\$130.5500
7/28/2021	Sold	-100	\$140.5300
7/28/2021	Sold	-103	\$140.5500
7/28/2021	Sold	-125	\$130.5400
7/28/2021	Sold	-125	\$130.5000
7/28/2021	Sold	-194	\$130.4800
7/28/2021	Sold	-200	\$130.5340
7/28/2021	Sold	-200	\$130.5300
7/28/2021	Sold	-240	\$140.5400
7/28/2021	Sold	-250	\$140.3700
7/28/2021	Sold	-379	\$140.4763
7/28/2021	Sold	-578	\$140.7900
7/28/2021	Sold	-856	\$130.6000
7/28/2021	Sold	-2,439	\$140.3600
8/16/2021	Bought	100	\$119.3300
8/20/2021	Bought	10	\$101.3100
8/23/2021	Bought	60	\$108.0600
8/24/2021	Bought	130	\$117.0000
8/27/2021	Sold	-300	\$53.2200
8/30/2021	Bought	20,100	\$95.0000
8/30/2021	Bought	400	\$52.5797
8/30/2021	Sold	-7,860	\$53.7400
8/30/2021	Sold	-12,240	\$53.6300
9/3/2021	Sold	-200	\$50.0000
9/7/2021	Sold	-200	\$49.5000
9/23/2021	Bought	150	\$56.4383
9/24/2021	Sold	-100	\$59.0000
9/27/2021	Bought	70	\$65.9250
9/28/2021	Sold	-120	\$63.4848

**Account 2**

<b>Date</b>	<b>Transaction Type</b>	<b>Quantity</b>	<b>Unit Price</b>
8/27/2021	Bought	200	\$90.0000
9/3/2021	Bought	100	\$50.0000
9/7/2021	Sold	-300	\$49.3487
9/23/2021	Bought	300	\$56.6900
9/27/2021	Sold	-300	\$59.0000

**Account 3**

<b>Date</b>	<b>Transaction Type</b>	<b>Quantity</b>	<b>Unit Price</b>
8/30/2021	Bought	600	\$85.0000
9/7/2021	Sold	-600	\$48.3230
9/23/2021	Bought	500	\$57.1980
9/24/2021	Sold	-500	\$59.0000

**Manohar K. Rao's Transactions in Cassava Sciences, Inc. Options****Account 1**

<b>Date</b>	<b>Transaction Type</b>	<b>Contract Type</b>	<b>Exp / Strike</b>	<b>Quantity</b>	<b>Price</b>
7/6/2021	Sold	Put	July 16, 2021 / \$70	-5	\$0.6500
7/6/2021	Sold	Put	July 16, 2021 / \$70	-3	\$0.6500
7/6/2021	Sold	Put	July 16, 2021 / \$70	-2	\$0.6500
7/6/2021	Sold	Put	July 16, 2021 / \$75	-5	\$1.5600
7/9/2021	Sold	Put	July 16, 2021 / \$95	-4	\$2.3000
7/12/2021	Sold	Put	July 16, 2021 / \$95	-6	\$3.4800
7/12/2021	Sold	Put	July 16, 2021 / \$90	-10	\$2.1500
7/12/2021	Sold	Put	July 16, 2021 / \$90	-20	\$2.1400
7/12/2021	Bought	Put	July 16, 2021 / \$90	30	\$1.9600
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-67	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-16	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-16	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-5	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-5	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-4	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-3	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-1	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$80	-1	\$0.6000
7/12/2021	Sold	Put	Jul 16, 2021 / \$85	-31	\$0.9500
7/12/2021	Sold	Put	Jul 16, 2021 / \$85	-20	\$1.1200
7/14/2021	Sold	Put	July 16, 2021 / \$95	-3	\$0.8100
7/14/2021	Sold	Put	July 16, 2021 / \$95	13	\$1.2400
7/14/2021	Sold	Put	Jul 16, 2021 / \$100	-12	\$3.1800
7/15/2021	Bought	Put	July 16, 2021 / \$70	10	\$0.2400
7/15/2021	Bought	Put	July 16, 2021 / \$75	5	\$0.3700
7/15/2021	Assigned	Put	Jul 16, 2021 / \$85	51	\$0.0000
7/16/2021	Bought	Put	Jul 16, 2021 / \$80	118	\$0.5000
7/19/2021	Sold	Put	Aug 20, 2021 / \$60	-21	\$5.7000
7/19/2021	Sold	Put	Aug 20, 2021 / \$60	-23	\$5.7000
7/19/2021	Sold	Put	Aug 20, 2021 / \$60	-12	\$5.7000

Date	Transaction Type	Contract Type	Exp / Strike	Quantity	Price
7/19/2021	Sold	Put	Aug 20, 2021 / \$60	-60	\$5.7000
7/19/2021	Sold	Put	Aug 20, 2021 / \$60	-44	\$5.7000
7/19/2021	Sold	Put	Aug 20, 2021 / \$60	-9	\$5.8000
7/19/2021	Sold	Put	Aug 20, 2021 / \$60	-6	\$5.8000
7/19/2021	Sold	Call	Aug 20, 2021 / \$100	-63	\$13.2700
7/19/2021	Assigned	Put	Jul 16, 2021 / \$100	12	\$0.0000
7/21/2021	Sold	Put	Aug 20, 2021 / \$80	-1	\$6.1000
7/21/2021	Sold	Put	Aug 20, 2021 / \$80	-1	\$6.1000
7/21/2021	Sold	Put	Aug 20, 2021 / \$80	-1	\$6.1000
7/21/2021	Sold	Put	Aug 20, 2021 / \$80	-8	\$6.1000
7/21/2021	Sold	Put	Aug 20, 2021 / \$80	-12	\$6.1000
7/22/2021	Sold	Put	Aug 20, 2021 / \$55	-1	\$1.4500
7/22/2021	Sold	Put	Aug 20, 2021 / \$55	-2	\$1.4700
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	100	\$1.6400
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	75	\$1.4500
7/23/2021	Bought	Call	Aug 20, 2021 / \$100	2	\$33.2000
7/23/2021	Bought	Put	Aug 20, 2021 / \$55	2	\$1.1500
7/23/2021	Bought	Put	Aug 20, 2021 / \$55	1	\$1.1300
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-1	\$4.0000
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-1	\$4.0000
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-1	\$4.0000
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-2	\$4.0000
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-2	\$4.0000
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-3	\$4.0000
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-13	\$3.9000
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-17	\$3.9200
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-44	\$4.0000
7/23/2021	Sold	Put	Aug 20, 2021 / \$80	-45	\$3.9000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	1	\$40.2500
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	4	\$40.2700
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	1	\$40.3000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	1	\$40.3400
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	11	\$40.3600
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	1	\$45.8000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	20	\$46.2000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	1	\$46.2000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	5	\$46.2000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	5	\$46.2000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	2	\$46.2000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	4	\$46.3000
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	3	\$45.8900
7/28/2021	Bought	Call	Aug 20, 2021 / \$100	2	\$45.9700
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	35	\$3.8000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	22	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	18	\$3.8000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	7	\$3.7900
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	7	\$3.8000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	7	\$3.8000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	7	\$3.8000

Date	Transaction Type	Contract Type	Exp / Strike	Quantity	Price
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	7	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	6	\$3.8000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	5	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	5	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	4	\$3.8000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	4	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	3	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	3	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	3	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	2	\$3.8000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	2	\$3.8000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	2	\$3.9000
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	1	\$3.7500
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	1	\$3.7800
7/28/2021	Bought	Put	Aug 20, 2021 / \$80	1	\$3.9000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-2	\$1.3500
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-2	\$1.3600
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-2	\$1.4000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-2	\$1.4000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-3	\$1.3000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-5	\$1.3500
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-8	\$1.4000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-9	\$1.4000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-12	\$1.3000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-14	\$1.4000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-18	\$1.3000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-25	\$1.3000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-29	\$1.4000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-30	\$1.3500
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-49	\$1.4000
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-53	\$1.3100
8/3/2021	Sold	Put	Aug 20, 2021 / \$55	-65	\$1.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	51	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	47	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	42	\$0.2500
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	37	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	24	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	23	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	23	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	21	\$0.2500
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	20	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	11	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	9	\$0.2500
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	7	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	5	\$0.2500
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	3	\$0.2400
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	2	\$0.2500
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	2	\$0.3000
8/11/2021	Bought	Put	Aug 20, 2021 / \$55	1	\$0.2500

Date	Transaction Type	Contract Type	Exp / Strike	Quantity	Price
8/11/2021	Sold	Put	Aug 20, 2021 / \$80	-5	\$1.0100
8/11/2021	Sold	Put	Aug 20, 2021 / \$90	-1	\$2.1000
8/11/2021	Sold	Put	Aug 20, 2021 / \$90	-1	\$2.1000
8/11/2021	Sold	Put	Aug 20, 2021 / \$90	-2	\$2.1000
8/11/2021	Sold	Put	Aug 20, 2021 / \$90	-2	\$2.1000
8/11/2021	Sold	Put	Aug 20, 2021 / \$90	-2	\$2.1000
8/11/2021	Sold	Put	Aug 20, 2021 / \$90	-3	\$2.1100
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-30	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-25	\$1.4000
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-25	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-24	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-23	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-16	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-16	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-11	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-9	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-5	\$1.4000
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-5	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-3	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-3	\$1.3500
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-2	\$1.4100
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-2	\$1.3600
8/11/2021	Sold	Put	Aug 20, 2021 / \$85	-1	\$1.3500
8/13/2021	Bought	Put	Aug 20, 2021 / \$80	3	\$0.6000
8/13/2021	Bought	Put	Aug 20, 2021 / \$80	1	\$0.5000
8/13/2021	Bought	Put	Aug 20, 2021 / \$80	1	\$0.6000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-3	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-4	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-4	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-6	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-6	\$0.9100
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-7	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-8	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-8	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-9	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-11	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-11	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-12	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-28	\$0.9000
8/13/2021	Sold	Put	Aug 20, 2021 / \$95	-63	\$0.9000
8/13/2021	Bought	Put	Aug 20, 2021 / \$85	1	\$0.8000
8/13/2021	Bought	Put	Aug 20, 2021 / \$85	2	\$0.8000
8/13/2021	Bought	Put	Aug 20, 2021 / \$85	9	\$0.8000
8/13/2021	Bought	Put	Aug 20, 2021 / \$85	19	\$0.8000
8/13/2021	Bought	Put	Aug 20, 2021 / \$85	26	\$0.8000
8/13/2021	Bought	Put	Aug 20, 2021 / \$85	35	\$0.8000
8/13/2021	Bought	Put	Aug 20, 2021 / \$85	51	\$0.8000
8/13/2021	Bought	Put	Aug 20, 2021 / \$85	57	\$0.8000
8/16/2021	Sold	Put	Aug 20, 2021 / \$90	-10	\$0.6700



Date	Transaction Type	Contract Type	Exp / Strike	Quantity	Price
8/16/2021	Sold	Call	Aug 20, 2021 / \$125	-1	\$5.9400
8/19/2021	Bought	Put	Aug 20, 2021 / \$90	21	\$1.4300
8/19/2021	Bought	Call	Aug 20, 2021 / \$125	1	\$0.3500
8/19/2021	Sold	Put	Aug 20, 2021 / \$95	-20	\$2.2300
8/19/2021	Sold	Call	Aug 27, 2021 / \$125	-1	\$5.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	121	\$0.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	27	\$0.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	19	\$0.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	9	\$0.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	9	\$0.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	5	\$0.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	4	\$0.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	3	\$0.3000
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	2	\$0.2900
8/20/2021	Bought	Put	Aug 20, 2021 / \$95	1	\$0.3000
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-4	\$0.7100
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-3	\$0.7000
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-26	\$0.7000
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-6	\$0.7000
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-4	\$0.6600
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-2	\$0.7000
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-1	\$0.6500
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-5	\$0.6500
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-1	\$0.6500
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-3	\$0.7000
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-91	\$0.6500
8/20/2021	Sold	Put	Aug 20, 2021 / \$100	-43	\$0.6500
8/20/2021	Expired	Put	Aug 20, 2021 / \$100	189	\$0.0000
8/23/2021	Sold	Put	Aug 27, 2021 / \$95	-87	\$1.1500
8/23/2021	Sold	Put	Aug 27, 2021 / \$95	-72	\$1.1500
8/23/2021	Sold	Put	Aug 27, 2021 / \$95	-39	\$1.2000
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-76	\$2.1500
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-26	\$1.9000
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-24	\$1.9700
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-18	\$2.0500
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-17	\$2.0600
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-15	\$1.9000
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-10	\$2.0000
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-8	\$2.1000
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-7	\$2.1000
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-6	\$2.1100
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-4	\$2.1700
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-4	\$2.1500
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-3	\$2.1600
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-2	\$2.1500
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-2	\$2.1000
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-1	\$1.9100
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-1	\$1.9000
8/23/2021	Bought	Put	Aug 27, 2021 / \$85	6	\$0.9500

Date	Transaction Type	Contract Type	Exp / Strike	Quantity	Price
8/23/2021	Bought	Put	Aug 27, 2021 / \$85	12	\$0.8500
8/23/2021	Bought	Put	Aug 27, 2021 / \$85	15	\$0.7500
8/23/2021	Bought	Put	Aug 27, 2021 / \$85	24	\$0.7200
8/23/2021	Bought	Put	Aug 27, 2021 / \$85	50	\$0.8000
8/23/2021	Bought	Put	Aug 27, 2021 / \$85	117	\$0.9000
8/24/2021	Sold	Put	Aug 27, 2021 / \$95	-6	\$0.8500
8/24/2021	Sold	Call	Aug 27, 2021 / \$125	-2	\$3.2400
8/25/2021	Bought	Call	Aug 27, 2021 / \$125	3	\$1.1000
8/27/2021	Bought	Put	Aug 27, 2021 / \$95	3	\$43.9200
8/30/2021	Assigned	Put	Aug 27, 2021 / \$95	201	\$0.0000
8/30/2021	Sold	Call	Sep 03, 2021 / \$60	-4	\$4.2300
9/1/2021	Sold	Call	Sep 03, 2021 / \$52	-4	\$3.1800
9/1/2021	Bought	Call	Sep 03, 2021 / \$60	4	\$1.0300
9/1/2021	Sold	Put	Sep 03, 2021 / \$35	-1	\$0.2000
9/1/2021	Sold	Put	Sep 03, 2021 / \$35	-15	\$0.1500
9/1/2021	Sold	Put	Sep 03, 2021 / \$40	-1	\$0.4500
9/1/2021	Sold	Put	Sep 03, 2021 / \$40	-1	\$0.4500
9/1/2021	Sold	Put	Sep 03, 2021 / \$40	-2	\$0.4500
9/1/2021	Sold	Put	Sep 03, 2021 / \$40	-2	\$0.4500
9/1/2021	Sold	Put	Sep 03, 2021 / \$40	-4	\$0.4500
9/3/2021	Sold	Call	Sep 03, 2021 / \$50	-4	\$0.3000
9/3/2021	Bought	Call	Sep 03, 2021 / \$52	4	\$0.5000
9/7/2021	Expired	Call	Sep 03, 2021 / \$50	2	\$0.0000
9/7/2021	Assigned	Call	Sep 03, 2021 / \$50	2	\$0.0000
9/7/2021	Expired	Put	Sep 03, 2021 / \$35	16	\$0.0000
9/7/2021	Expired	Put	Sep 03, 2021 / \$40	10	\$0.0000
9/22/2021	Sold	Call	Sep 24, 2021 / \$59	-1	\$1.1600
9/24/2021	Assigned	Call	Sep 24, 2021 / \$59	1	\$0.0000
10/13/2021	Sold	Put	Oct 15 2021 / \$42	-14	\$0.1000
10/13/2021	Bought	Put	Oct 15 2021 / \$46	48	\$0.1600
10/13/2021	Sold	Put	Oct 15 2021 / \$46	-34	\$0.1000
10/13/2021	Sold	Put	Oct 15 2021 / \$46	-14	\$0.1000
10/14/2021	Bought	Put	Oct 15 2021 / \$42	14	\$0.1500
11/19/2021	Sold	Put	Nov 26 2021 / \$30	-69	\$0.1300
11/19/2021	Sold	Put	Nov 26 2021 / \$30	-1	\$0.1500
11/26/2021	Expired	Put	Nov 26 2021 / \$30	70	\$0.0000
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-56	\$0.0600
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-62	\$0.0500
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-21	\$0.0500
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-17	\$0.0500
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-13	\$0.0500
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-8	\$0.0500
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-7	\$0.0500
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-7	\$0.0500
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-2	\$0.1000
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-4	\$0.0500
11/26/2021	Sold	Put	Dec 03 2021 / \$30	-3	\$0.0500
11/30/2021	Bought	Put	Dec 03 2021 / \$30	1	\$0.1000
11/30/2021	Bought	Put	Dec 03 2021 / \$30	11	\$0.1500

Date	Transaction Type	Contract Type	Exp / Strike	Quantity	Price
11/30/2021	Bought	Put	Dec 03 2021 / \$30	18	\$0.1500
11/30/2021	Bought	Put	Dec 03 2021 / \$30	17	\$0.1500
11/30/2021	Bought	Put	Dec 03 2021 / \$30	20	\$0.1400
11/30/2021	Bought	Put	Dec 03 2021 / \$30	22	\$0.1500
11/30/2021	Bought	Put	Dec 03 2021 / \$30	5	\$0.1500
11/30/2021	Bought	Put	Dec 03 2021 / \$30	92	\$0.1500
11/30/2021	Bought	Put	Dec 03 2021 / \$30	7	\$0.1500
11/30/2021	Bought	Put	Dec 03 2021 / \$30	7	\$0.1500

## Account 2

Date	Transaction Type	Contract Type	Exp / Strike	Quantity	Price
7/12/2021	Sold	Put	Jul 16, 2021 / \$85	-2	\$0.9100
7/16/2021	Bought	Put	Jul 16, 2021 / \$85	2	\$1.4200
7/22/2021	Sold	Put	Aug 20, 2021 / \$55	-2	\$1.5300
7/22/2021	Sold	Put	Aug 20, 2021 / \$55	-1	\$1.5000
8/13/2021	Bought	Put	Aug 20, 2021 / \$55	3	\$0.2600
8/13/2021	Sold	Put	Aug 20, 2021 / \$100	-2	\$1.7500
8/20/2021	Expired	Put	Aug 20, 2021 / \$100	2	\$0.0000
8/23/2021	Sold	Put	Aug 27, 2021 / \$90	-2	\$2.6000
8/30/2021	Assigned	Put	Aug 27, 2021 / \$90	2	\$0.0000
8/30/2021	Sold	Call	Sep 03, 2021 / \$60	-2	\$3.5000
8/30/2021	Sold	Put	Sep 03, 2021 / \$50	-1	\$1.6500
8/31/2021	Bought	Call	Sep 03, 2021 / \$60	2	\$1.0700
8/31/2021	Sold	Call	Sep 03, 2021 / \$51	-2	\$3.7100
9/3/2021	Assigned	Put	Sep 03, 2021 / \$50	1	\$0.0000
9/3/2021	Expired	Call	Sep 03, 2021 / \$51	2	\$0.0000
9/22/2021	Sold	Call	Sep 24, 2021 / \$59	-3	\$1.1000
9/24/2021	Assigned	Call	Sep 24, 2021 / \$59	3	\$0.0000
9/24/2021	Sold	Put	Oct 01, 2021 / \$55	-3	\$0.8500
9/27/2021	Bought	Put	Oct 01, 2021 / \$55	3	\$0.5700

## Account 3

Date	Transaction Type	Contract Type	Exp / Strike	Quantity	Price
7/12/2021	Sold	Put	Jul 16, 2021 / \$85	-23	\$1.0800
7/16/2021	Bought	Put	Jul 16, 2021 / \$85	23	\$1.5400
7/19/2021	Sold	Put	Aug 20, 2021 / \$60	-33	\$5.9000
7/22/2021	Sold	Put	Aug 20, 2021 / \$50	-2	\$1.0800
7/22/2021	Sold	Put	Aug 20, 2021 / \$50	-1	\$1.0700
7/23/2021	Bought	Put	Aug 20, 2021 / \$50	3	\$1.1000
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	2	\$1.6500
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	2	\$1.6500
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	3	\$1.6500
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	3	\$1.6500
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	3	\$1.6500
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	3	\$1.6500
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	5	\$1.6500
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	5	\$1.6500

<b>Date</b>	<b>Transaction Type</b>	<b>Contract Type</b>	<b>Exp / Strike</b>	<b>Quantity</b>	<b>Price</b>
7/23/2021	Bought	Put	Aug 20, 2021 / \$60	7	\$1.6500
8/20/2021	Sold	Put	Aug 20, 2021 / \$101	-5	\$1.1500
8/20/2021	Expired	Put	Aug 20, 2021 / \$101	5	\$0.0000
8/23/2021	Sold	Put	Aug 27, 2021 / \$85	-6	\$2.5100
8/30/2021	Assigned	Put	Aug 27, 2021 / \$85	6	\$0.0000
8/30/2021	Sold	Call	Sep 03, 2021 / \$60	-6	\$3.4800
8/31/2021	Sold	Put	Sep 03, 2021 / \$50	-1	\$1.8100
9/1/2021	Sold	Call	Sep 03, 2021 / \$52	-6	\$3.1900
9/1/2021	Bought	Call	Sep 03, 2021 / \$60	6	\$1.1100
9/1/2021	Bought	Put	Sep 03, 2021 / \$50	1	\$2.2700
9/7/2021	Expired	Call	Sep 03, 2021 / \$52	6	\$0.0000
9/22/2021	Sold	Call	Sep 24, 2021 / \$59	-5	\$1.3400
9/22/2021	Assigned	Call	Sep 24, 2021 / \$59	5	\$0.0000
9/24/2021	Sold	Put	Oct 01, 2021 / \$55	-6	\$0.8600
9/27/2021	Bought	Put	Oct 01, 2021 / \$55	6	\$0.6000